UNCLASSIFIED

THIS PAGE IS UNCLASSIFIED

AD_____

GRANT NUMBER DAMD17-95-1-5002

TITLE: Database of Autotransplants for Breast Cancer

PRINCIPAL INVESTIGATOR: Mary M. Horowitz, M.D.

CONTRACTING ORGANIZATION: Medical College of Wisconsin
                          Milwaukee, Wisconsin 53226

REPORT DATE: December 1997

TYPE OF REPORT: Annual

PREPARED FOR: Commander
              U.S. Army Medical Research and Materiel Command
              Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Distribution authorized to U.S. Government
agencies only (proprietary information, Dec 97). Other requests
for this document shall be referred to U.S. Army Medical Research
and Materiel Command, 504 Scott Street, Fort Detrick, Maryland
21702-5012.

The views, opinions and/or findings contained in this report are
those of the author(s) and should not be construed as an official
Department of the Army position, policy or decision unless so
designated by other documentation.

19980526 075

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE December 1997	3. REPORT TYPE AND DATES COVERED Annual (1 Nov 96 – 31 Oct 97)

4. TITLE AND SUBTITLE
Database of Autotransplants for Breast Cancer

5. FUNDING NUMBERS
DAMD17-95-1-5002

6. AUTHOR(S)
Mary M. Horowitz, M.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Medical College of Wisconsin
Milwaukee, Wisconsin 53226

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, MD 21702-5012

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT

Distribution authorized to U.S. Government agencies only (proprietary information, Dec 97). Other requests for this document shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200*

The Autologous Blood and Marrow Transplant Registry (ABMTR) is a voluntary organization of over 200 autotransplant centers that contribute clinical data on consecutive autotransplant recipients to a Statistical Center at the Medical College of Wisconsin. The ABMTR's database includes information for more than 11,000 women receiving autotransplants for breast cancer. According to data reported to the ABMTR, breast cancer is the most common indication for blood and marrow transplantation (allogeneic or autologous) in North America. The current contract facilitates numerous enhancements to the ABMTR's clinical database, statistical support services and informational programs. These include collection of socioeconomic and clinical data on women receiving autotransplants for breast cancer and institutional data on centers doing transplants, streamlining data entry and management, development of appropriate statistical techniques for analyzing posttransplant data, and expansion of programs to provide access to collected data for patients, physicians and others involved in caring for women with breast cancer.

14. SUBJECT TERMS Breast Cancer, Autologous Transplants, Bone Marrow Transplant, Peripheral Blood Stem Cells, High Dose Therapy, Survival Analysis

15. NUMBER OF PAGES
351

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Limited

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

_____ Where copyrighted material is quoted, permission has been obtained to use such material.

_MW_ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

_MW_ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

_____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

_____ For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

_____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

_____ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

_____ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

PI - Signature   4/26/97 Date

3

TABLE OF CONTENTS

Grant Number: DAMD17-95-1-5002
Database of Autotransplants for Breast Cancer

<u>Appendices</u>

Appendix 1   ABMTR Report Forms
Appendix 2   ABMTR Participating Centers and ABMTR Breast Cancer Working Committee
Appendix 3   1997 and 1998 Data Management Sessions
Appendix 4   Publications
Appendix 5   Statisticians' Manual
Appendix 6   ABMTR Newsletters, including 1996 IBMTR/ABMTR Summary Slides
Appendix 7   World Wide Web Pages
Appendix 8   Presentations on Breast Cancer

INTRODUCTION

Use of high-dose therapy with autologous blood or bone marrow hematopoietic support (autotransplants) to treat breast cancer continues to increase. According to data reported to the Autologous Blood and Marrow Transplant Registry (ABMTR), breast cancer was the most common indication for allogeneic or autologous blood or marrow transplantation in 1996. The ABMTR maintains a large database of clinical information on persons receiving autotransplants. This database provides important information relevant to breast cancer treatment. The purpose of the work funded in this contract was 1.) to enhance the existing ABMTR database so that important unresolved issues in use of autotransplants to treat breast cancer could be addressed and accurate information on autotransplants could be provided to women with breast cancer; and, 2.) to develop and make available appropriate biostatistical models for analyzing this database. Considerable progress was made during the first two years of this contract including development of revised data collection forms, development of software for distributed data entry, computerization of log-in processes, planning and initiating a survey of transplant center characteristics, completion of one large study of autotransplants in breast cancer and initiation of several others, evaluation of statistical models, direct provision of data to patients and clinicians, presentation of data to national societies and organizations involved in planning breast cancer research, and planning a World Wide Web site with information related to autotransplants for breast cancer. Progress continued during the third year of this grant with analysis of data obtained on the institutional survey, planning for conversion to a more modern and versatile database platform, completion of several statistical and clinical studies, documentation of study proposal and analysis procedures and further development of World Wide Web educational materials. Progress in each of the Technical Objectives outlined in our contract proposal is outlined below.

PROGRESS IN ACHIEVING TECHNICAL OBJECTIVES

1.0 *Develop and enhance an observational database for autotransplants in breast cancer, including demographic, clinical, treatment, financial, and outcome data.*

1.1 Data collection

ABMTR centers are required to register all consecutive autotransplants with the ABMTR Statistical Center. Registration data include age, sex, race, disease stage and duration, graft type, graft treatment, conditioning regimen, graft treatment, and posttransplant disease status, survival and second cancers. Registration data allow analysis of trends in transplant use and outcome and identification of patients for specific studies. Comprehensive data are collected on a subset of these cases using the ABMTR Report Forms developed during Year 1 of this contract (Appendix 1). Data collection for 1994-1997 is summarized in Table 1.1.

Table 1.1 Accrual of autotransplants to the ABMTR database, 1994-1997.

Dates	Registration data		Report data	
	All diseases	Breast cancer	All diseases	Breast cancer
7/94 - 6/95	4,804	1,857	1594	637
7/95 - 6/96	5,414	2,256	1955	958
7/96 - 6/97	5,611	2,461	2923	1,044
TOTAL	15,829	5,896	6472	2,639

Two hundred twenty-two centers participate in the ABMTR Research Program (Appendix 2). The ABMTR now has registration data for 11,535 and comprehensive data for 3,770 recipients of autotransplants for breast cancer. The database is longitudinal; centers are requested to provide follow-up on survivors yearly.

As noted, data collection instruments (Report Forms) were revised during the first year of this contract and distributed in August 1995 (Appendix 1). Report Form enhancements were described in previous progress reports. The result of these enhancements and continued accrual of patients is a database with greater capabilities to address multiple issues relevant to breast cancer treatment. These data are increasingly used for timely clinical studies (see Section 4.0 below).

1.2 Uniform reporting of data

During the second year of this contract, work began on a revised Data Manual to accompany the new Report Forms. The revised Manual was distributed for review during the current contract year. Substantial modifications were requested by users and are in progress. A final version will be available in early 1998.

In January 1997, the ABMTR conducted a two-day training session for data managers, in conjunction with the ABMTR Annual Meeting in Scottsdale, Arizona (see Meeting Program and Evaluation Summary in Appendix 3). One hundred twenty-five persons attended; 49 of these received travel grants to partially offset expenses of attending (see list of grantees in Appendix 3). These travel grants, which are given preferentially to first time attendees, allow many persons to attend who would not otherwise be able to participate. Participants indicated a high level of satisfaction with the topics covered and training provided.

1.3   Data review and entry

Currently, about 15% of ABMTR centers register patients by submitting data on disc rather than paper. Statistical Center personnel continue to work on conversion programs to accommodate multiple data formats. During the second year of the contract, we computerized the log-in procedure for paper Report Forms to allow electronic comparison with data previously supplied on Registration. This provided verification of key fields; all discrepancies are resolved with the reporting center. During the current contract year, these programs were further developed and log-in procedures were streamlined. Thus, despite handling larger numbers of reports and verifying key fields, the lag time between Report Form receipt and log-in decreased from six to 1-2 months. Additionally, in the third year of the contract, we continued our work with StemCell Technologies to develop software for distributed data entry. Approximately 150 centers have purchased StemSoft software and about 40 now use StemSoft to enter data and generate (paper) IBMTR/ABMTR forms. Software (BMTLink) to directly convert data entered on StemSoft software to a computerized format appropriate for incorporation in the IBMTR/ABMTR database was developed in cooperation with StemCell and is being tested at the Statistical Center on data from a limited number of transplant centers. Further modifications are required before this software can be widely implemented but, once implemented, it will allow data entry to be done completely at transplant centers, submitted on disk and incorporated into the database after appropriate error, consistency and virus checks. This will result in substantial savings in effort and cost by the Statistical Center.

1.4   Data validation

An Audit Schema was developed and approved in 1995. Audits reveal a high level of accuracy for reported data and no evidence of selective reporting. Audit procedures were extensively reviewed at the 1997 Annual Meeting. Guidelines for auditors and for evaluation of audit reports were subsequently developed.

1.5   Computer capabilities

Our efforts to allow electronic data submission are outlined in Section 1.2 above. During the past two years, the inadequacy of Scientific Information Retrieval (SIR), which has been the Statistical Center's database platform since 1980, to meet the challenges of collecting and managing an ever increasing volume of data has become apparent. Although it served the Statistical Center's needs well for many years, SIR has not kept pace with developments in database technology over the past 3-5 years. Limitations include: the user interface is character-based rather than graphical; no screen painters or report painters are available and development of screens and entry-time validation is done through a non-standard command language; there is no mechanism for defining multi-step transactions or automatic maintenance of relationships between tables; and, there is no mechanism to access SIR databases directly from third party analysis or applications development software, preventing us from using powerful tools available from other

vendors. Declining availability of technical support and software upgrades are additional problems. Consequently, a review of currently available database software was done during the current grant year to assess new platforms. A preliminary plan for conversion of the IBMTR/ABMTR database from the current SIR to Oracle was developed. This included a careful analysis of data flow patterns, reimbursement tracking and communications between the Statistical Center and participating transplant centers as well as extensive error and validity checking. Preliminary work on this project is in progress.

2.0   *Identify institutional characteristics of centers performing autotransplants for breast cancer in the United States and Canada, including academic affiliation, patient volume, physician training, staff/patient ratio.*

The institutional survey designed in Year 1 was completed. Initial analysis of responses was done in collaboration with the American Society for Blood and Marrow Transplantation which also conducted a survey of U.S. transplant centers focusing on monitoring high-dose chemotherapy administration (see confidential preprint in Appendix 4). Additional analyses of these data are in progress.

3.0   *Evaluate and develop statistical models and software for effectively analyzing transplant data.*

Statistical Center faculty have explored the following aspects of statistical analysis of transplantation data:

> 3.1   <u>Proportional hazards regression with random groups effects</u>. Frailty models are used in survival analysis to model unobserved heterogeneity or to model group effects (e.g. center effects). The model for group effects assumes that, conditional on a random effect, individuals within a group follow a standard proportional hazards model multiplied by the random effect. Common models for the random effect are the gamma distribution, the inverse Gaussian distribution, and the positive stable model. We have developed SAS macros to fit these three models. The macros are available at the Division of Biostatistics Website (www.biostat.mcw.edu).

> 3.2   <u>Accelerated failure time models with random effects</u>. To date, all models for random effects are based on a multiplicative model for the effect of frailty on the conditional hazard rate. Drs. John Klein and Mei-Jie Zhang at the ABMTR Statistical Center have studied an alternative model in which an accelerated failure time model is assumed, conditional on the frailty. The common frailty in a group either adds or subtracts a common amount from each group member's log survival times. Assuming a Gaussian distribution for the frailty and for the log survival times, this leads to a multivariate normal model for the life lengths within a group. Maximum likelihood estimates of the model parameters are obtained for this model and the properties of the model are studied. A paper discussing this approach will appear in *Biometrics*.

3.2   Joint modeling of the number of transfusions and time to death. Drs. Klein and Hee-Chang Park (Changwon National University, South Korea) have looked at models for the number of transfusions a patient receives after transplant. The models look at joint models for numbers of transfusions and death times. Weibull models are assumed for the event times and Poisson models are assumed for the counts. The counts and event times are assumed to be independent given random effects which affect either the event time and/or the counts. In a paper under review for *Biometrics*, a common random effect is assumed and maximum likelihood estimates of the model parameters is assumed. This model allows one to study the effects of covariates on the counts and event times, to estimate the expected number of transfusions a patient may have at a given time, and to study the effects of the number on transfusions on survival. Alternative models to the common random effects model have been studied. These include models where the random effects are different for the counts and the event time, but these random effects are themselves correlated. These models are important for studying hematopoietic recovery after high-dose therapy. A paper discussing this model is currently being prepared.

3.3   Comparison of statistical tests for center effects. Drs. Klein, Zhang and Per Andersen (University of Copenhagen) have completed a Monte Carlo study of methods for testing for the presence of a center effect following a Cox regression analysis. The study compared an approach which treats center effects as fixed versus an approach which treats center effects as random. Random effects were tested using a score test. The study found that the random effects test worked quite well for small to moderate samples when either the random effects or fixed effects model held true. For the fixed effects model, larger sample sizes were required. When the sample size was small (<10 per center), the fixed effects model falsely rejected the hypothesis of a center effect when there was an effect. This study has important implications for analysis of multi-center trials. The results are in a manuscript under review for *Statistics in Medicine.*

3.4   Models for excess and relative mortality. Drs. Klein and Zhang have studied techniques for comparing the mortality rates of transplant patients with standard published mortality rates. As opposed to existing techniques, these models allow for the incorporation of risk factors for transplant. Two models are considered. The first is the model for relative mortality. In this model the arbitrary baseline hazard rate in the Cox model is replaced by the known population hazard rate. The second is a model for excess mortality. Here a modification of the additive hazards model is used. Both models allow for point and interval estimates of the time after transplant when a transplant recipient with a given set of risk factors has a mortality rate which has returned to that in the reference population. This is important in studying long-term survivors of cancer treatment.

3.5   Confidence regions for the times when two survival curves are different. Drs. Klein and Zhang have developed procedures to determine a confidence region for the times at which two treatments are different. The regions are based on either an assumed proportional hazards analysis or on an additive hazards regression model. Both models allow for the adjustment of fixed covariates. This is important when comparing treatments with different time patterns of adverse events. A paper discussing these methods is to appear in the *Journal of Planning and Inference.*

3.6   Multistate modeling in survival analysis. Dr. Klein has studied techniques for modeling the recovery process after a transplant as a dynamic function of intermediate events occurring after transplantation. The model can be used to provide a prediction of a patients ultimate prognosis at any point in time given the patient's history up to that time. With Dr. Qain (Ohio State University) a number of semi-parametric models and analyses have been developed. This material has appeared in the *Proceedings of the ASA Conference*. With a Ph.D. student from the University of Wisconsin, Dr. Klein is examining modifications of these models which allow for the incorporation of random effects.

3.7   General statistical analysis. Dr. Klein has authored a book chapter for the volume, *Clinical Bone Marrow and Stem Cell Transplantation: Reference Textbook* which surveys statistical procedures commonly used in transplantation. He has also written an article for the *Encyclopedia of Statistics* on "Survival Distributions and their Characteristics." Dr. Zhang has contributed two short articles to the *Encyclopedia of Biostatistics* on techniques for grouped survival data. Dr. Klein, with Prof. Richard Johnson of the University of Wisconsin has authored an article for the *Handbook of Biostatistics* on regression techniques for censored (survival) data.

4.0   ***Provide access to data and biostatistical support for clinical studies related to autotransplants in breast cancer.***

During the first year of this contract, the ABMTR Working Committee completed its first review of use and outcome of autotransplants for breast cancer. This paper was published in the *Journal of Clinical Oncology* in May 1997 (Appendix 4). Other studies completed or in progress are:

4.1   Prognostic factors in autotransplants for metastatic breast cancer. *(Study chair: K. Antman, Columbia University, New York City; Study statistician: S.C. Murphy, ABMTR).* We analyzed data for 1,188 consecutive women receiving autotransplants for metastatic breast cancer in North America. Transplants were performed in 63 institutions between 1989 and 1995. The 2-year probability of survival was $42 \pm 3\%$ and progression-free survival, $18 \pm 2\%$. Multivariate analyses identify older age, Karnofsky performance score $< 90\%$, absence of estrogen receptors, metastases developing <18 months after adjuvant therapy, resistance to chemotherapy pretransplant, and more than two sites of disease or liver or central nervous system involvement as predictors of poor outcome. There is no significant difference in outcome among the most frequently used conditioning regimens. A manuscript is in preparation.

4.2   Comparison of autotransplants with conventional chemotherapy for metastatic breast cancer. *(Study chairs: D. Berry, CALGB, Duke University; P.A. Rowlings, ABMTR; Study statistician: D. Berry, CALGB).* To date only one small (n=90 women) randomized trial has compared outcome of conventional therapy with autotransplants for metastatic breast cancer. This showed a modest survival advantage for autotransplants in women with newly diagnosed metastatic breast cancer. The validity and generalizeability of this results has been questioned. We are using the data set described in 4.1 above to

10

study this issue in a large group of women by comparing autotransplants with conventional therapy of women treated on protocols of the Cancer and Leukemia Group B (CALGB). Statistical techniques and the detailed patient-level data available for these patients were used to adjust for differences in patient- and disease-related characteristics between the cohorts. A file with data for 1,481 women was provided to Dr. Don Berry, CALGB statistician. Analyses are in progress.

4.3   Prognostic factors in autotransplants for Stage II/III Breast Cancer. *(Study chair: E. Reed, University of Nebraska, Omaha; Study statistician: S.C. Murphy, ABMTR).* In 1990, only 15% of autotransplants for breast cancer were in women with Stage II/III disease; in 1995 45% were for early stage disease. The ABMTR is studying outcome of autotransplants for 689 women with Stage II/III breast cancer to determine outcome and identify prognostic factors. Median age was 43 (range, 28-66) years. Median number of involved axillary nodes was 12 (range, 0-46). More than 90% of women received an anthracycline-based chemotherapy regimen prior to high-dose therapy. The most commonly used conditioning regimens were cyclophosphamide and thiotepa (CT, 40%) and CT plus carboplatin (20%). Three-year probability of survival was $72 \pm 9\%$. In multivariate analyses, use of posttransplant hormone therapy for persons with estrogen receptor positive tumors, use of pre- or posttransplant local radiation therapy and a short interval between diagnosis and transplant were associated with better outcome. These data were presented at the meeting of the American Society for Clinical Oncology in May 1997, Denver. Additional analyses are in progress.

4.4   Autotransplants in men with breast cancer. *(Study chair: P. McCarthy, Roswell Park Cancer Institute, Buffalo; Study statistician: S.C. Murphy, ABMTR).* Breast cancer is rare in men. Consequently, there are few data regarding results of autotransplant for men with breast cancer. We studied 14 men receiving autotransplants for breast cancer reported to the ABMTR. Five had stage 2 breast cancer, 2 had stage 3 breast cancer, 2 had stage 3-inflammatory breast cancer, and 4 had metastatic breast cancer. For one patient receiving an autotransplant as adjuvant therapy, initial stage was uncertain. Ten of 12 tumors tested were estrogen receptor positive. Median age at transplant was 50 years. All patients had hematopoietic recovery. There was no major regimen-related toxicity. Of 10 men receiving autotransplants as adjuvant therapy, 2 relapsed 10 and 13 months posttransplant and subsequently died 16 and 19 months posttransplant. Eight of 10 are disease-free with median follow-up of 11 (range 6-37) months. Of 4 men treated for metastatic breast cancer, 2 had persistent or recurrent disease and 2 are disease-free 5 and 9 months posttransplant. Results appear similar to those reported for women receiving autotransplants for breast cancer. A manuscript is in preparation and will be submitted shortly.

4.5   Assessment of variation in costs of autotransplants for breast cancer among institutions. *(Study chair: C. Bennett, Northwestern University, Chicago; Study statistician: T. Waters, Northwestern University, Chicago).* Preliminary data on more than 800 patients transplanted in four centers were analyzed. These data suggest that costs of autotransplants for breast cancer are significantly less than costs for transplants for hematologic malignancies. Data collection from 10 additional centers is in progress.

4.6   Determination of second cancer risk after autotransplants for breast cancer. *(Study chair: M.M. Horowitz, ABMTR Statistical Center; Study statistician: R. Curtis, National Cancer Institute)* Increased surveillance for second cancers was part of several efforts at supplemental data collection under this contract. Centers registering second cancers are now asked to supply diagnostic information on Supplemental New Malignancy Forms (Appendix 1). We have identified 14 second primary breast cancers and 35 cancers of other types (10 leukemia/myelodysplasias, 6 cancers of the female genital tract, 4 skin cancers, 3 lung cancers, 2 thyroid cancers and 11 other cancers) thus far. Comparison of second cancer risk in women receiving autotransplants for breast cancer versus an age-, sex- and race-matched general population is planned.

All of these studies are enhanced by the improved data collection, entry and management funded by this contract and by the greater level of detail now available on transplant recipients. Awareness of the resources of data and statistical expertise available through the Statistical Center is steadily increasing as are proposals to use the database for clinical research. To clearly delineate the procedures for proposing and conducting studies, Statistical Center staff developed a Statistician's Manual for studies using Registry data and statistical personnel (Appendix 5). This document helps focus study proposals, ensure that data handling and analysis are of high quality and ensure that the expertise of Registry Working Committees (Appendix 2) is fully utilized.

5.0   *Disseminate information regarding autotransplants for breast cancer to patients, physicians and others involved in care of women with breast cancer.*

The ABMTR database is a unique resource of information regarding use and outcome of transplants, containing data not readily available in the medical literature. Summary statistics on the use and outcome of autotransplants for breast cancer were included in the November 1996 issue of the ABMTR Newsletter (Appendix 6), which is widely distributed to transplant and oncology centers. An updated version of these data is also available on-line at the IBMTR/ABMTR homepage on the World Wide Web (address: www.biostat.mcw.edu/IBMTR; Appendix 7). There were at least 12 presentations of ABMTR data related to use and/or outcome of autotransplants for breast cancer during the third contract year (Appendix 8).

Additionally during the third contract year, the ABMTR, through its Information Resource program (partially funded by this contract) provided information regarding use and outcome of autotransplants for breast cancer in response to about 275 specific requests from physicians, patients and health-related agencies or companies. Data provided in response to these requests often included survival and other outcome data not readily available in the medical literature.

In addition to the IBMTR/ABMTR homepage, and in collaboration with the National Marrow Donor Program and the American Society of Blood and Marrow Transplantation, the ABMTR has developed a World Wide Web site with comprehensive information on the role of transplantation in treating various cancers. The site includes general transplant information, disease-specific information, and an "Ask the Expert" page where users may post questions which will be triaged to appropriate persons for response. A comprehensive review of the role of high-dose chemotherapy in treating breast cancer is among the first topics to be made available. The Website will be open to the public in December 1997 at the following address:

http://www.bmtinfo.org. Hard copies of pages relevant to breast cancer are enclosed in Appendix 7. Information is provided at basic (the average lay person) and technical (general physician or sophisticated lay person) levels, with an extensive bibliography aimed at transplant physicians that will be updated periodically, and with links to other relevant Web sites providing information on transplantation and cancer.

CONCLUSIONS AND FUTURE PLANS

This contract continues to facilitate numerous enhancements to the ABMTR database and Statistical Center. It is already elevating the quality of information available for studies and for health care providers and consumers. By completion of the four-year term of this award, we are confident that these infrastructure enhancements will lead to numerous high-quality investigations.

IBMTR / ABMTR

APPENDICES

Grant No. DAMD17-95-1-5002

"Database of Autotransplants for Breast Cancer"

Submitted to: U.S. Army Medical Research and Material Command

December 1, 1997

MEDICAL COLLEGE OF WISCONSIN

CORE FORM	FOR REGISTRY USE ONLY:

I.D. ☐ – ☐☐☐☐☐ – ☐☐☐☐☐☐

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

(Institutional Unique Blood or Marrow Transplant Identification Number)

Date received:

Registry: IBMTR   ABMTR   *(circle one)*

Date of transplant for which this form is being completed: ☐☐ ☐☐ ☐☐
Month Day Year

Date of report: ☐☐ ☐☐ ☐☐
Month Day Year

IBMTR
International Bone Marrow Transplant Registry

Series 095 Reporting Forms

IBMTR/ABMTR

ABMTR
North America
Autologous Blood & Marrow Transplant Registry

Statistical Center • Medical College of Wisconsin
P.O. Box 26509 • 8701 Watertown Plank Road • Milwaukee, WI 53226
Telephone: 414-456-8325 • Fax: 414-266-8471

Demographics

---

* If this is a report of a second (or subsequent) transplant check here ☐ and go to Q.20

1. Institutional protocol number *(if applicable)*: ☐☐☐☐☐☐☐☐☐☐☐☐

2. Was patient enrolled in cooperative group (eg. CALGB, CCSG, EBMT, ECOG, EORTC, MRC, NSABP, POG, SWOG, etc.) study at any time or reported to the NMDP or EBMT? *(include transplant and non-transplant studies)*

1 ☐ Yes
0 ☐ No
8 ☐ Unknown

Study 1:	**3.** Group _____	**4.** Study No. _____	**5.** Patient No. _____
Study 2:	**6.** Group _____	**7.** Study No. _____	**8.** Patient No. _____
Study 3:	**9.** Group _____	**10.** Study No. _____	**11.** Patient No. _____

12. Sex: 1 ☐ Male   2 ☐ Female

13. Race: *(If patient's parents are from two separate groups of the following, check both)*

Caucasian/White
11 ☐ European or Western Russia
12 ☐ Middle East or North Coast of Africa
10 ☐ White, not otherwise specified

Black
21 ☐ African American
22 ☐ African Black (both parents born in Africa)
23 ☐ Caribbean Black
24 ☐ South or Central American Black
20 ☐ Black, not otherwise specified

Asian/Pacific Islander
31 ☐ Asian Indian
32 ☐ Filipino
33 ☐ Hawaiian (Polynesian)
34 ☐ Japanese
35 ☐ Korean
36 ☐ Northern Chinese
37 ☐ Southeast Asian/ Southern Chinese
30 ☐ Oriental, not otherwise specified

Hispanic
41 ☐ Caribbean Hispanic
42 ☐ Mexican or Southwestern USA Hispanic

43 ☐ South or Central American Hispanic
40 ☐ Hispanic, not otherwise specified

Native American
51 ☐ Native Alaskan/ Eskimo/Aleut
52 ☐ American Indian
50 ☐ Native American, not otherwise specified

Other
90 ☐ Other, specify:
_____
88 ☐ Unknown

14. Date of birth: ☐☐ ☐☐ ☐☐
Month Day Year

Disease

15. What was the primary disease for which transplant was performed?
(*Appropriate Insert must be submitted with this form*)

10 ☐ Acute myelogenous leukemia (AML or ANLL) —

- 11 ☐ M1, myeloblastic
- 12 ☐ M2, myelocytic
- 13 ☐ M3, promyelocytic (APML, APL)
- 14 ☐ M4, myelomonocytic
- 15 ☐ M5, monocytic
- 16 ☐ M6, erythroblastic
- 17 ☐ M7, megakaryoblastic
- 18 ☐ Granulocytic sarcoma
- 19 ☐ Other, specify:

  _____

- 10 ☐ Unknown

> *Complete Insert I and continue with Question 17 on Page 5*

20 ☐ Acute lymphoblastic leukemia (ALL) —

- 21 ☐ Mature B-cell (L3)
- 22 ☐ T-cell
- 23 ☐ Null cell (early Pre-B)
- 24 ☐ cALLa (includes Pre-B)
- 29 ☐ Other, specify:

  _____

- 20 ☐ Unknown

> *Complete Insert II and continue with Question 17 on Page 5*

40 ☐ Chronic myelogenous leukemia (CML) —

- 41 ☐ Ph¹ +; BCR/ABL+
- 42 ☐ Ph¹ +; BCR/ABL -
- 43 ☐ Ph¹ +; BCR/ABL unknown
- 44 ☐ Ph¹ -; BCR/ABL +
- 45 ☐ Ph¹ -; BCR/ABL -
- 46 ☐ Ph¹ -; BCR/ABL unknown
- 47 ☐ Ph¹ unknown; BCR/ABL +
- 48 ☐ Ph¹ unknown; BCR/ABL -
- 49 ☐ Other, specify:

  _____

- 40 ☐ Ph¹ unknown; BCR/ABL unknown

> *Complete Insert III and continue with Question 17 on Page 5*

30 ☐ Other leukemia —

- 34 ☐ Chronic lymphocytic leukemia (CLL)

  > *Complete Insert IV and continue with Question 17 on Page 5*

- 31 ☐ Acute undifferentiated leukemia
- 32 ☐ Biphenotypic, bilineage or hybrid leukemia
- 33 ☐ Acute mast cell leukemia
- 35 ☐ Hairy cell leukemia
- 36 ☐ Juvenile CML (no evidence of Philadelphia chromosome or BCR/ABL)
- 37 ☐ Prolymphocytic leukemia (PLL)
- 38 ☐ M0, stem cell
- 39 ☐ Other, specify:

  _____

- 30 ☐ Unknown

> *Continue with Question 16 on Page 5*

50 ☐ Myelodysplastic/ myeloproliferative disorders (*please classify all preleukemias*)

(*If patient has transformed to AML, complete Insert I and indicate AML as the primary disease*)

- 51 ☐ Refractory anemia (RA)
- 52 ☐ Refractory anemia with excess blasts (RAEB)
- 53 ☐ Refractory anemia with excess blasts in transformation (RAEBT)
- 54 ☐ Chronic myelomonocytic leukemia (CMML)
- 55 ☐ Acquired idiopathic sideroblastic anemia (RARS)
- 56 ☐ Paroxysmal nocturnal hemoglobinuria (PNH)
- 57 ☐ Polycythemia vera
- 58 ☐ Essential or primary thrombocythemia
- 59 ☐ Myelofibrosis with myeloid metaplasia
- 60 ☐ Other myelofibrosis or myelosclerosis
- 69 ☐ Other myelodysplasia or myeloproliferative disorder, specify:

  _____

- 50 ☐ Unknown

> *Complete Insert V and continue with Question 17 on Page 5*

100 ☐ Non-Hodgkin lymphoma —

- 101 ☐ Small cell lymphocytic
- 102 ☐ Follicular, predominantly small cleaved cell
- 103 ☐ Follicular, mixed, small cleaved and large cell
- 104 ☐ Follicular, predominantly large cell
- 105 ☐ Diffuse, small cleaved cell
- 106 ☐ Diffuse, mixed, small and large cell
- 107 ☐ Diffuse, large cell
- 108 ☐ Large cell, immunoblastic
- 109 ☐ Lymphoblastic
- 110 ☐ Small noncleaved cell, unclassified
- 111 ☐ Small noncleaved cell, Burkitt
- 112 ☐ Small noncleaved cell, non-Burkitt
- 113 ☐ Mycosis fungoides
- 114 ☐ Histiocytic
- 115 ☐ Mantle cell/ intermediate differentiation
- 116 ☐ Composite, specify:

  _____
- 117 ☐ Large cell anaplastic lymphoma, Ki1 positive
- 118 ☐ Primary CNS lymphoma
- 119 ☐ Other non-Hodgkin lymphoma, specify:

  _____
- 100 ☐ Non-Hodgkin lymphoma, unknown

Complete Insert VI and continue with Question 17 on Page 5

150 ☐ Hodgkin lymphoma —

- 151 ☐ Lymphocyte predominant
- 152 ☐ Nodular sclerosis
- 153 ☐ Mixed cellularity
- 154 ☐ Lymphocyte depleted
- 159 ☐ Other Hodgkin lymphoma, specify:

  _____
- 150 ☐ Hodgkin lymphoma, unknown

Complete Insert VI and continue with Question 17 on Page 5

170 ☐ Multiple myeloma/ Plasma cell disorder —

- 171 ☐ Multiple myeloma

  Complete Insert VII and continue with Question 17 on Page 5
- 172 ☐ Plasma cell leukemia
- 173 ☐ Waldenstrom macroglobulinemia
- 174 ☐ Amyloidosis
- 175 ☐ Solitary plasmacytoma
- 179 ☐ Other, specify:

  _____

Continue with Question 16 on Page 5

200 ☐ Other malignancies —

- 250 ☐ Breast cancer

  Complete Insert VIII and continue with Question 17 on Page 5
- 201 ☐ Head & neck cancer
- 202 ☐ Lung cancer, small cell
- 203 ☐ Lung cancer, non-small cell
- 239 ☐ Lung, not otherwise specified
- 204 ☐ Mediastinal neoplasm, specify:

  _____
- 205 ☐ GI tract cancer
- 206 ☐ Pancreatic cancer
- 207 ☐ Hepatobiliary cancer
- 208 ☐ Kidney & urinary tract cancer
- 209 ☐ Prostate cancer
- 210 ☐ Testicular cancer
- 211 ☐ External genitalia cancer
- 212 ☐ Cervical cancer
- 213 ☐ Uterine cancer
- 214 ☐ Ovarian (epithelial) cancer
- 215 ☐ Vaginal cancer
- 216 ☐ Sarcoma unspecified
- 217 ☐ Soft tissue sarcoma
- 218 ☐ Bone sarcoma (not Ewing)
- 219 ☐ Melanoma
- 220 ☐ Central nervous system tumor
- 221 ☐ Wilm tumor
- 222 ☐ Neuroblastoma
- 223 ☐ Retinoblastoma
- 224 ☐ Ewing sarcoma
- 269 ☐ Other malignancy, specify:

  _____

Continue with Question 16 on Page 5

300 ☐ Severe aplastic anemia —

- 301 ☐ Idiopathic
- 302 ☐ Secondary to hepatitis
- 303 ☐ Secondary to toxin/other drug
- 304 ☐ Amegakaryocytosis (not congenital)
- 309 ☐ Other, specify:

Complete Insert IX and continue with Question 17 on Page 5

310 ☐ Inherited abnormalities of erythrocyte differentiation or function —

(If patient has developed leukemia, complete Insert for appropriate leukemia diagnosis)

- 311 ☐ Fanconi anemia

  Complete Insert X and continue with Question 17 on Page 5
- 312 ☐ Diamond-Blackfan anemia (pure red cell aplasia)
- 319 ☐ Other, specify:

  _____

Complete Insert IX and continue with Question 17 on Page 5

310 ☐ Inherited abnormalities of erythrocyte differentiation or function, *continued*

- 350 ☐ Thalassemia major (β thalassemia), unspecified
- 351 ☐ Type A Thalassemia major
- 352 ☐ Type B+ Thalassemia major
- 353 ☐ Type B0 Thalassemia major
- 354 ☐ Type BE Thalassemia major
- 355 ☐ Sickle Thalassemia major
- 356 ☐ Sickle cell anemia
- 359 ☐ Other hemoglobinopathy, specify:

  _____
- 310 ☐ Unknown

  Complete Insert XI and continue with Question 17 on Page 5

400 ☐ SCID and other disorders of the immune system

- 401 ☐ ADA deficiency severe combined immunodeficiency (SCID)
- 402 ☐ Absence of T and B cells SCID
- 403 ☐ Absence of T, normal B cell SCID
- 404 ☐ Omenn syndrome
- 405 ☐ Reticular dysgenesis
- 406 ☐ Bare lymphocyte syndrome
- 419 ☐ SCID other, specify:

  _____
- 451 ☐ Ataxia telangiectasia
- 452 ☐ HIV infection
- 454 ☐ DiGeorge anomaly
- 455 ☐ Chronic granulomatous disease
- 456 ☐ Chediak-Higashi syndrome
- 457 ☐ Common variable immunodeficiency
- 458 ☐ X-linked lymphoproliferative syndrome
- 459 ☐ Leukocyte adhesion deficiencies, including GP180, CD-18, LFA and WBC adhesion deficiencies
- 460 ☐ Kostmann agranulocytosis (congenital neutropenia)
- 461 ☐ Neutrophil actin deficiency
- 462 ☐ Cartilage-hair hypoplasia
- 470 ☐ Combined immunodeficiency disease (CID), unspecified
- 474 ☐ CID other, specify: _____
- 479 ☐ Other immunodeficiencies, specify: _____

  Complete Insert XII and continue with Question 17 on Page 5
- 453 ☐ Wiskott Aldrich syndrome

  Complete Insert XIII and continue with Question 17 on Page 5

500 ☐ Inherited abnormalities of platelets

- 501 ☐ Amegakaryocytosis/ congenital thrombocytopenia
- 502 ☐ Glanzmann thrombasthenia
- 509 ☐ Other, specify: _____

  Continue with Question 16 on Page 5

520 ☐ Inherited disorders of metabolism

- 521 ☐ Osteopetrosis (malignant infantile osteopetrosis)

  Complete Insert XV and continue with Question 17 on Page 5
- 522 ☐ Lesch-Nyhan

Mucopolysaccharidosis
- 531 ☐ Hurler syndrome (IH)
- 532 ☐ Scheie syndrome (IS)
- 533 ☐ Hunter syndrome (II)
- 534 ☐ Sanfilippo (III)
- 535 ☐ Morquio (IV)
- 536 ☐ Maroteaux-Lamy (VI)
- 537 ☐ β-glucuronidase deficiency (VII)
- 538 ☐ Mucopolysaccharidosis (V)
- 539 ☐ Other mucopolysaccharidosis, specify: _____
- 530 ☐ Mucopolysaccharidosis, not otherwise specified

Mucolipidoses
- 541 ☐ Gaucher disease
- 542 ☐ Metachromatic leukodystrophy
- 543 ☐ Adrenoleukodystrophy
- 544 ☐ Krabbe disease (globoid leukodystrophy)
- 545 ☐ Neiman-Pick disease
- 546 ☐ I-cell disease
- 547 ☐ Wolman disease
- 548 ☐ Glucose storage disease
- 549 ☐ Lysosomal storage disease
- 559 ☐ Other mucolipidoses, specify:

  _____
- 540 ☐ Mucolipidoses, not otherwise specified
- 529 ☐ Other specific inherited metabolic disorders, specify:

  _____
- 520 ☐ Unknown

  Complete Insert XIV and continue with Question 17 on Page 5

570 ☐ Histiocytic disorders

- 571 ☐ Familial erythrophagocytic lymphohistiocytosis (FEL, Familial hemophagocytic lymphohistiocytosis)
- 572 ☐ Histiocytosis-X
- 573 ☐ Hemophagocytosis
- 574 ☐ Malignant histiocytosis
- 579 ☐ Other, specify: _____
- 570 ☐ Unknown

  Continue with Question 16 on Page 5

900 ☐ Other

Specify: _____

_____

Continue with Question 16 on Page 5

Clinical Status of Patient Prior to Conditioning

16. Date of diagnosis of primary disease:
(complete only if a disease-specific Insert is not required)
☐☐ ☐☐ ☐☐
Month Day Year

17. *Allografts only:* Patient's blood type:

1 ☐ A Positive	5 ☐ A Negative	9 ☐ A Rh unknown	88 ☐ Unknown
2 ☐ B Positive	6 ☐ B Negative	10 ☐ B Rh unknown	
3 ☐ AB Positive	7 ☐ AB Negative	11 ☐ AB Rh unknown	
4 ☐ O Positive	8 ☐ O Negative	12 ☐ O Rh unknown	

18. Has patient ever been pregnant?

1 ☐ Yes ————
0 ☐ No
8 ☐ Unknown
7 ☐ Not applicable (patient is male, or a female child)

> **19.** Number of pregnancies: ☐☐

20. Did patient receive blood transfusions at any time prior to conditioning?

1 ☐ Yes ————
0 ☐ No
8 ☐ Unknown

> **21.** Give number (best estimate) of donor exposures:
>
> | | |
> |---|---|
> | 1 ☐ 1 - 5 | 5 ☐ 31 - 40 |
> | 2 ☐ 6 - 10 | 6 ☐ 41 - 50 |
> | 3 ☐ 11 - 20 | 7 ☐ > 50 |
> | 4 ☐ 21 - 30 | 8 ☐ Unknown |

22. What was the functional status of patient prior to conditioning?

> *If the patient is 16 years of age or older, complete the Karnofsky Scale. If patient is younger than 16 years of age, complete the Lansky Scale. Rate activity of patient immediately prior to initiation of conditioning.*

Karnofsky Scale (age ≥16 yrs)

Select the phrase in the Karnofsky Scale which best describes the activity status of the patient:

Able to carry on normal activity; no special care is needed.
- ☐100 Normal; no complaints; no evidence of disease
- ☐ 90 Able to carry on normal activity
- ☐ 80 Normal activity with effort

Unable to work; able to live at home, care for most personal needs; a varying amount of assistance is needed.
- ☐ 70 Cares for self; unable to carry on normal activity or to do active work
- ☐ 60 Requires occasional assistance but is able to care for most needs
- ☐ 50 Requires considerable assistance and frequent medical care

Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.
- ☐ 40 Disabled; requires special care and assistance
- ☐ 30 Severely disabled; hospitalization indicated, although death not imminent
- ☐ 20 Very sick; hospitalization necessary
- ☐ 10 Moribund; fatal process progressing rapidly

Lansky Scale (age <16 yrs)

Select the phrase in the Lansky Play-Performance Scale which best describes the activity status of the patient:

Normal range.
- ☐100 Fully active
- ☐ 90 Minor restriction in physically strenuous play
- ☐ 80 Restricted in strenuous play, tires more easily, otherwise active

Mild to moderate restriction.
- ☐ 70 Both greater restrictions of, and less time spent in, active play
- ☐ 60 Ambulatory up to 50% of time, limited active play with assistance/supervision
- ☐ 50 Considerable assistance required for any active play; fully able to engage in quiet play

Moderate to severe restriction.
- ☐ 40 Able to initiate quiet activities
- ☐ 30 Needs considerable assistance for quiet activity
- ☐ 20 Limited to very passive activity initiated by others (i.e., TV)
- ☐ 10 Completely disabled, not even passive play

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

23. Was there clinically significant coexisting disease or organ impairment prior to conditioning?

1 ☐ Yes ——

0 ☐ No

What were the diagnoses?

    Yes No

24. 1☐ 0☐ Significant *hemorrhage* (e.g. CNS or GI), specify site(s): _____

_____

Cardiovascular

25. 1☐ 0☐ Coronary artery disease

26. 1☐ 0☐ Hypertension

27. 1☐ 0☐ Other cardiac disease, specify:_____

Endocrine

28. 1☐ 0☐ Diabetes mellitus

29. 1☐ 0☐ Thyroid disease

30. 1☐ 0☐ Other endocrine disease, specify:_____

CNS

31. 1☐ 0☐ Seizure disorder

32. 1☐ 0☐ Other CNS disease, specify:_____

Pulmonary

33. 1☐ 0☐ Asthma

34. 1☐ 0☐ Other pulmonary disease, specify:_____

35. 1☐ 0☐ *Genitourinary* disease, specify:_____

36. 1☐ 0☐ *Gastrointestinal* disease, specify:_____

37. 1☐ 0☐ *Hematologic* disease, specify:_____

Chromosomal

38. 1☐ 0☐ Fanconi anemia

39. 1☐ 0☐ Down syndrome

40. 1☐ 0☐ Other chromosomal disorders, specify:_____

41. 1☐ 0☐ History of *other malignancy*, specify:_____

42. 1☐ 0☐ *Neonatal GVHD*

Autoimmune disease

43. 1☐ 0☐ Rheumatoid arthritis

44. 1☐ 0☐ Systemic lupus erythematosis

45. 1☐ 0☐ Multiple sclerosis

46. 1☐ 0☐ Polyarteritis nodosa

47. 1☐ 0☐ Psoriasis

48. 1☐ 0☐ Other autoimmune disease, specify:_____

49. 1☐ 0☐ *Other*, specify:_____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

Organ Function Prior to Conditioning

Provide values for patient's liver function just prior to conditioning:

		Date tested:				What is the upper limit of normal for your institution?
		Month	Day	Year		

50. AST (SGOT) ☐☐☐ . U/L   51. ☐☐ ☐☐ ☐☐   52. ☐☐☐ . U/L

53. ALT (SGPT) ☐☐☐ . U/L   54. ☐☐ ☐☐ ☐☐   55. ☐☐☐ . U/L

56. Total serum bilirubin ☐☐☐ . ☐   58. ☐☐ ☐☐ ☐☐   59. ☐☐☐ . ☐

> 57. Unit of measurement for bilirubin:
> 1 ☐ mg/dL   2 ☐ μmol/L

60. LDH ☐☐☐☐☐ . U/L   61. ☐☐ ☐☐ ☐☐   62. ☐☐☐☐ . U/L

63. Did patient have known clinical liver disease (eg. viral hepatitis) at any time prior to conditioning?

1 ☐ Yes
0 ☐ No

> | | Yes | No | Unknown | |
> |---|---|---|---|---|
> | 64. | 1 ☐ | 0 ☐ | 8 ☐ | Hepatitis B |
> | 65. | 1 ☐ | 0 ☐ | 8 ☐ | Hepatitis A |
> | 66. | 1 ☐ | 0 ☐ | 8 ☐ | Hepatitis C |
> | 67. | 1 ☐ | 0 ☐ | 8 ☐ | Drug toxicity |
> | 68. | 1 ☐ | 0 ☐ | 8 ☐ | Other, specify: _____ |
>
> 69. Date of onset: ☐☐ ☐☐   ☐ Date Unknown
>   Month Year

70. What was patient's serum creatinine prior to conditioning?   ☐☐☐ . ☐

Date tested:
72. ☐☐ ☐☐ ☐☐
    Month Day Year

> 71. Unit of measurement for creatinine:
> 1 ☐ mg/dL   2 ☐ μmol/L

73. Patient smokes cigarettes, or has in the past:

1 ☐ Yes
0 ☐ No
8 ☐ Unknown

> 74. Average number of packs per day: ☐ . ☐
>
> 75. Number of years: ☐☐

76. Was clinically important infection(s) present or being treated <u>within one week prior to conditioning</u>?
Note: Report later infections on page 30 of this report.

1 ☐ Yes

0 ☐ No

Select site and organism from lists shown on the next page and place number in the appropriate spaces. If more than one site or organism were involved, list one site of infection and organism on the first line, second site and/or organism on second line.

		Site	Organism
77. ☐ Bacterial <u>Typical</u>	First	**78.** ☐☐	**79.** _____
	Second	**80.** ☐☐	**81.** _____
<u>Atypical</u>	First	**83.** ☐☐	**84.** B☐☐☐
	Second	**85.** ☐☐	**86.** B☐☐☐

87. Other atypical bacterium, specify:_____

88. ☐ Fungal	First	**89.** ☐☐	**90.** F☐☐☐
	Second	**91.** ☐☐	**92.** F☐☐☐

93. Other fungus, specify: _____

94. ☐ Viral	First	**95.** ☐☐	**96.** V☐☐☐
	Second	**97.** ☐☐	**98.** V☐☐☐

99. Other virus, specify:_____

100. ☐ Parasitic	First	**101.** ☐☐	**102.** P☐☐☐
	Second	**103.** ☐☐	**104.** P☐☐☐

105. Other parasite, specify:_____

106. ☐ No organism identified	First	**107.** ☐☐	**108.** O509
	Second	**109.** ☐☐	**110.** O509

Codes for Common Sites of Infection

01	Blood / buffy coat	40	*Genito-Urinary Tract unspecified*
02	Disseminated – generalized, isolated at 3 or more distinct sites	41	Kidneys, renal pelvis, ureters and bladder
03	*Central Nervous System unspecified*	42	Prostate
04	Brain	43	Testes
05	Spinal cord	44	Fallopian tubes, uterus, cervix
06	Meninges and CSF	45	Vagina
10	*Gastrointestinal Tract unspecified*	50	*Skin unspecified*
11	Lips	51	Genital area
12	Tongue, oral cavity and oro-pharynx	52	Cellulitis
13	Esophagus	53	Herpes Zoster
14	Stomach	54	Rash, pustules or abscesses not typical of any of the above
15	Gallbladder and biliary tree (not hepatitis), pancreas	60	Central venous catheter, not otherwise specified
16	Small intestine	61	Catheter insertion site
17	Large intestine	62	Catheter tip
18	Feces/stool	70	Eyes
19	Peritoneum	75	Ear
20	Liver	80	*Other unspecified*
30	*Respiratory unspecified*	81	Joints
31	Upper airway and nasopharynx	82	Bone marrow
32	Laryngitis/larynx	83	Bone cortex (osteomyelitis)
33	Lower respiratory tract (lung)	84	Muscle (excluding cardiac)
34	Pleural cavity, pleural fluid	85	Cardiac (endocardium, myocardium, pericardium)
35	Sinuses	86	Lymph nodes
		87	Spleen

Codes for Commonly Reported Organisms

1. Bacteria

(Indicate code for atypical bacteria; list bacterium for non-atypical bacteria.)

100	Atypical bacteria, not otherwise specified
101	Coxiella
102	Legionella
103	Leptospira
104	Listeria
105	Mycoplasma
106	Nocardia
107	Rickettsia
110	Tuberculosis, NOS (AFB, acid fast bacillus, Koch bacillus)
111	Typical tuberculosis (TB, Tuberculosis)
112	Mycobacteria (avium, bovium, intracellulare)
113	Chlamydia
119	Other atypical bacteria, specify

2. Fungal Infections

200	Candida, not otherwise specified
201	Candida albicans
202	Candida krusei
203	Candida parapsilosis
204	Candida tropicalis
205	Torulopsis glabrata (a subspecies of candida)
209	Candida, other
210	Aspergillus, not otherwise specified
211	Aspergillus flavus
212	Aspergillus fumigatus
213	Aspergillus niger
219	Aspergillus, other
220	Cryptococcus species
230	Fusarium species
240	Mucormycosis (zygomycetes, rhizopus)
250	Yeast, not otherwise specified
259	Other fungus, specify

3. Viral Infections

301	Herpes Simplex (HSV1, HSV2)
302	Herpes Zoster (Chicken pox, Varicella)
303	Cytomegalovirus (CMV)
304	Adenovirus
305	Enterovirus (Coxsackie, Echo, Polio)
306	Hepatitis A (HAV)
307	Hepatitis B (HBV, Australian antigen)
308	Hepatitis C (HCV)
309	HIV-1 (HTLV-III)
310	Influenza
311	Measles (Rubeola)
312	Mumps
313	Papovavirus
314	Respiratory syncytial virus (RSV)
315	Rubella (German Measles)
316	Parainfluenza
317	Human herpesvirus-6 (HHV-6)
318	Epstein-Barr virus (EBV)
319	Polyomavirus
320	Rotavirus
321	Rhinovirus
329	Other viral, specify

4. Parasite Infections

401	Pneumocystis (PCP)
402	Toxoplasma
403	Giardia
404	Cryptosporidium
409	Other parasite (amebiasis, echinococcal cyst, trichomonas – either vaginal or gingivitis), specify

5. Other Infections

509	No organism identified

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

112. Did patient have a history of clinically important <u>fungal</u> infection <u>at any time</u> prior to conditioning for transplant?

1 ☐ Yes

0 ☐ No

113. Date of onset:

☐☐ ☐☐
Month Year

114. Select organism from list on previous page:

F☐☐ If other, specify: _____

Select site(s) from list on previous page:

115. ☐☐ **116.** ☐☐ Other, specify: _____

Tests for Serological Evidence of Prior Viral Exposure / Infection

	Positive	Negative	Inconclusive	Not Tested
117. HTLV1 antibody	1 ☐	2 ☐	3 ☐	4 ☐
118. Toxoplasma antibody	1 ☐	2 ☐	3 ☐	4 ☐
119. Cytomegalovirus antibody	1 ☐	2 ☐	3 ☐	4 ☐
120. Epstein-Barr antibody	1 ☐	2 ☐	3 ☐	4 ☐
121. Hepatitis B surface and/or core antibody	1 ☐	2 ☐	3 ☐	4 ☐
122. Hepatitis B surface antigen	1 ☐	2 ☐	3 ☐	4 ☐
123. Hepatitis C antibody	1 ☐	2 ☐	3 ☐	4 ☐
124. Hepatitis A antibody	1 ☐	2 ☐	3 ☐	4 ☐
125. Human Immunodeficiency Virus (HIV) antibody	1 ☐	2 ☐	3 ☐	4 ☐

7 ☐ Not able to release information for HIV

High-Dose Therapy (Pretransplant Conditioning)

126. Was patient given high-dose therapy (conditioning) as an inpatient?

1 ☐ Yes

0 ☐ No, given as outpatient

7 ☐ No high dose therapy given

127. Was patient treated in an isolation room during the peri-transplant period?

1 ☐ Yes

0 ☐ No

Please specify:

	Yes	No	
128.	1 ☐	0 ☐	Conventional private room
129.	1 ☐	0 ☐	Laminar air flow room
130.	1 ☐	0 ☐	HEPA filtered room
131.	1 ☐	0 ☐	Positive pressure
132.	1 ☐	0 ☐	Other, specify:

133. Date pretransplant conditioning (radiation or drugs) was begun:

☐☐ ☐☐ ☐☐
Month Day Year

134. Height at initiation of pretransplant conditioning (without shoes): ☐☐☐ cm

135. Weight at initiation of pretransplant conditioning (without shoes): ☐☐☐ kg

136. Was irradiation performed as part of the pretransplant conditioning regimen? 1 ☐ Yes 0 ☐ No —[Go to Q. 182]

137. Source of x-ray therapy:
  1 ☐ Linear accelerator 2 ☐ ⁶⁰Co 7 ☐ Other, specify: _____

> **138.** Maximum energy: ☐☐☐ MV (million volts)

139. Calculated mid-line dose-rate during irradiation: ☐☐.☐ cGy (rad)/min

What was the radiation field?

140. Total Body Radiation 1 ☐ Yes ———
  0 ☐ No

> **141.** Total dose: ☐☐☐☐ cGy
>
> Prescription point:
>   Yes No
> **142.** 1☐ 0☐ Midline umbilicus
> **143.** 1☐ 0☐ Other, specify: _____
>
> Patient orientation:
>   Yes No
> **144.** 1☐ 0☐ AP/PA
> **145.** 1☐ 0☐ Other, specify: _____
>
> Method of dose verification:
>   Yes No
> **146.** 1☐ 0☐ Phantom
> **147.** 1☐ 0☐ Diodes on patient
> **148.** 1☐ 0☐ Other, specify: _____
>
> **149.** Starting date: ☐☐ ☐☐ ☐☐
>   Month Day Year
>
> **150.** Was radiation fractionated?
>   1 ☐ Yes ———
>   0 ☐ No
>   8 ☐ Unknown
>
> > **151.** Dose per fraction: ☐☐☐☐ cGy
> > **152.** Number of days: ☐☐
> > **153.** Total number of fractions: ☐☐
>
> **154.** Was shielding used?
>   1 ☐ Yes ———
>   0 ☐ No
>   8 ☐ Unknown
>
> >   Yes No
> > **155.** 1☐ 0☐ Lungs
> > **156.** 1☐ 0☐ Eyes
> > **157.** 1☐ 0☐ Liver
> > **158.** 1☐ 0☐ Kidney
> > **159.** 1☐ 0☐ Other, specify:
> > _____

[*Radiation field data continued on next page*]

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

160. Total lymphoid or nodal regions 1 ☐ Yes ———┐
0 ☐ No

161. Total dose: ☐☐☐☐ cGy **162.** Starting date: ☐☐ ☐☐ ☐☐
Month Day Year

163. Was radiation fractionated?

1 ☐ Yes ———
0 ☐ No
8 ☐ Unknown

164. Dose per fraction: ☐☐☐☐ cGy

165. Number of days: ☐☐

166. Total number of fractions: ☐☐

167. Thoraco-abdominal region 1 ☐ Yes ———┐
0 ☐ No

168. Total dose: ☐☐☐☐ cGy **169.** Starting date: ☐☐ ☐☐ ☐☐
Month Day Year

170. Was radiation fractionated?

1 ☐ Yes ———
0 ☐ No
8 ☐ Unknown

171. Dose per fraction: ☐☐☐☐ cGy

172. Number of days: ☐☐

173. Total number of fractions: ☐☐

174. Other radiation field 1 ☐ Yes ———┐
0 ☐ No

175. Specify field: _____

176. Total dose: ☐☐☐☐ cGy **177.** Starting date: ☐☐ ☐☐ ☐☐
Month Day Year

178. Was radiation fractionated?

1 ☐ Yes ———
0 ☐ No
8 ☐ Unknown

179. Dose per fraction: ☐☐☐☐ cGy

180. Number of days: ☐☐

181. Total number of fractions: ☐☐

182. Was (additional) radiation given to other sites?

1 ☐ Yes

0 ☐ No

183. Was CNS irradiation performed?

1 ☐ Yes — **184.** Dose: ☐☐☐☐ cGy **185.** Date started: ☐☐ ☐☐ ☐☐

0 ☐ No Month Day Year

186. Was gonadal irradiation performed?

1 ☐ Yes — **187.** Dose: ☐☐☐☐ cGy **188.** Date started: ☐☐ ☐☐ ☐☐

0 ☐ No Month Day Year

189. Was splenic irradiation performed?

1 ☐ Yes — **190.** Dose: ☐☐☐☐ cGy **191.** Date started: ☐☐ ☐☐ ☐☐

0 ☐ No Month Day Year

192. Other site, specify: _____

1 ☐ Yes — **193.** Dose: ☐☐☐☐ cGy **194.** Date started: ☐☐ ☐☐ ☐☐

0 ☐ No Month Day Year

195. Were drugs given for <u>pretransplant</u> conditioning? 1 ☐ Yes 0 ☐ No — [Go to Q. 361]

196. Date started: ☐☐ ☐☐ ☐☐
  Month Day Year

	Drug Given No Yes	Total dose (in mg) pre-marrow infusion (not daily dose)	Number of doses	Continuous infusion Yes No	Number of days
197. ALG, ALS, ATG, ATS	0 ☐ 1 ☐ — **198.**	☐☐☐☐☐	**199.** ☐	**200.** 1 ☐ 0 ☐	**201.** ☐
202. Anthracycline (0 ☐ No 1 ☐ Yes)					
203. Daunomycin	0 ☐ 1 ☐ — **204.**	☐☐☐☐☐	**205.** ☐	**206.** 1 ☐ 0 ☐	**207.** ☐
208. Doxorubicin (Adriamycin)	0 ☐ 1 ☐ — **209.**	☐☐☐☐☐	**210.** ☐	**211.** 1 ☐ 0 ☐	**212.** ☐
213. Idarubicin	0 ☐ 1 ☐ — **214.**	☐☐☐☐☐	**215.** ☐	**216.** 1 ☐ 0 ☐	**217.** ☐
218. Rubidazone	0 ☐ 1 ☐ — **219.**	☐☐☐☐☐	**220.** ☐	**221.** 1 ☐ 0 ☐	**222.** ☐
223. Other anthra-cycline, specify: _____	0 ☐ 1 ☐ — **224.**	☐☐☐☐☐	**225.** ☐	**226.** 1 ☐ 0 ☐	**227.** ☐
228. Bleomycin	0 ☐ 1 ☐ — **229.**	☐☐☐☐☐	**230.** ☐	**231.** 1 ☐ 0 ☐	**232.** ☐
233. Busulfan (myleran)	0 ☐ 1 ☐ — **234.**	☐☐☐☐☐	**235.** ☐	**236.** 1 ☐ 0 ☐	**237.** ☐
238. Carboplatin	0 ☐ 1 ☐ — **239.**	☐☐☐☐☐	**240.** ☐	**241.** 1 ☐ 0 ☐	**242.** ☐
243. Cisplatin	0 ☐ 1 ☐ — **244.**	☐☐☐☐☐	**245.** ☐	**246.** 1 ☐ 0 ☐	**247.** ☐

Continued on next page

	Drug Given	Total dose (in mg) pre-marrow infusion	Number of doses	Continuous infusion	Number of days
	No Yes				

248. Corticosteroids [0 ☐ No 1 ☐ Yes]

249. Methylprednisolone (Solumedrol)

Yes No

1 ☐ Yes — [250. ☐ Oral ☐ IV] — 251. ☐☐☐☐☐ 252. ☐ 253. 1 ☐ 0 ☐ 254. ☐

0 ☐ No

255. Prednisone 0 ☐ 1 ☐ —— 256. ☐☐☐☐☐ 257. ☐ 258. 1 ☐ 0 ☐ 259. ☐

260. Dexamethasone 0 ☐ 1 ☐ —— 261. ☐☐☐☐☐ 262. ☐ 263. 1 ☐ 0 ☐ 264. ☐

265. Other cortico-steroids, specify: 0 ☐ 1 ☐ —— 266. ☐☐☐☐☐ 267. ☐ 268. 1 ☐ 0 ☐ 269. ☐

_____

270. Cyclophosphamide 0 ☐ 1 ☐ —— 271. ☐☐☐☐☐ 272. ☐ 273. 1 ☐ 0 ☐ 274. ☐

275. Cytarabine (Ara-C) 0 ☐ 1 ☐ —— 276. ☐☐☐☐☐ 277. ☐ 278. 1 ☐ 0 ☐ 279. ☐

280. Etoposide (VP16) 0 ☐ 1 ☐ —— 281. ☐☐☐☐☐ 282. ☐ 283. 1 ☐ 0 ☐ 284. ☐

285. Ifosfamide 0 ☐ 1 ☐ —— 286. ☐☐☐☐☐ 287. ☐ 288. 1 ☐ 0 ☐ 289. ☐

290. **Intrathecal chemotherapy** [0 ☐ No 1 ☐ Yes]

291. Cytarabine 0 ☐ 1 ☐ —— 292. ☐☐☐☐☐ 293. ☐   294. ☐

295. Methotrexate 0 ☐ 1 ☐ —— 296. ☐☐☐☐☐ 297. ☐   298. ☐

299. Other, specify: 0 ☐ 1 ☐ —— 300. ☐☐☐☐☐ 301. ☐   302. ☐

_____

303. Melphalan (L-PAM)

1 ☐ Yes — [304. ☐ Oral ☐ IV] —— 305. ☐☐☐☐☐ 306. ☐ 307. 1 ☐ 0 ☐ 308. ☐

0 ☐ No

309. Mitoxantrone 0 ☐ 1 ☐ —— 310. ☐☐☐☐☐ 311. ☐ 312. 1 ☐ 0 ☐ 313. ☐

314. **Monoclonal antibody** [0 ☐ No 1 ☐ Yes]

315. Radionuclide-tagged Mab, specify: 0 ☐ 1 ☐ —— 316. ☐☐☐☐☐ 317. ☐ 318. 1 ☐ 0 ☐ 319. ☐

_____

320. Campath 0 ☐ 1 ☐ —— 321. ☐☐☐☐☐ 322. ☐ 323. 1 ☐ 0 ☐ 324. ☐

325. Other Mab, specify: 0 ☐ 1 ☐ —— 326. ☐☐☐☐☐ 327. ☐ 328. 1 ☐ 0 ☐ 329. ☐

Continued on next page

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐☐

	Drug Given No Yes	Total dose (in mg) pre-marrow infusion	Number of doses	Continuous infusion Yes No	Number of days
330. Nitrosourea (0☐ No 1☐ Yes)					
331. BCNU	0☐ 1☐ ——— 332.	☐☐☐☐☐	333. ☐	334. 1☐ 0☐	335. ☐
336. CCNU	0☐ 1☐ ——— 337.	☐☐☐☐☐	338. ☐	239. 1☐ 0☐	340. ☐
341. Other nitrosourea, specify:	0☐ 1☐ ——— 342.	☐☐☐☐☐	343. ☐	344. 1☐ 0☐	345. ☐
_____					
Paclitaxel (Taxol)	0☐ 1☐ ———	☐☐☐☐☐	☐	1☐ 0☐	☐
346. Teniposide (VM26)	0☐ 1☐ ——— 347.	☐☐☐☐☐	348. ☐	349. 1☐ 0☐	350. ☐
351. Thiotepa	0☐ 1☐ ——— 352.	☐☐☐☐☐	353. ☐	354. 1☐ 0☐	355. ☐
356. Other, specify:	0☐ 1☐ ——— 357.	☐☐☐☐☐	358. ☐	359. 1☐ 0☐	360. ☐
_____					

361. Was this the first transplant for this recipient?

1☐ Yes ———

0☐ No

> **362.** Is a second transplant planned as part of treatment protocol? 1☐ Yes ———
>
> 0☐ No —— (Go to Q. 384)

363. Number of previous transplants recipient has had: ☐☐

(if more than 1 previous transplant, photocopy Q.364–383 and answer for each previous transplant)

Continued on next page

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐☐

364. Date of previous transplant: ☐☐ ☐☐ ☐☐
                                     Month Day Year

365. Graft type of previous transplant:

1 ☐ **Autologous** ─────
                  Yes No
           366. 1☐ 0☐ Bone marrow
           367. 1☐ 0☐ Peripheral blood
           368. 1☐ 0☐ Other, specify: _____

           369. Was this transplant reported to the ABMTR – North America?
                  1 ☐ Yes ───── ABMTR I.D. ☐☐☐☐☐☐☐
                  0 ☐ No
                  8 ☐ Unknown

2 ☐ **Allogeneic,** ─────
    unrelated
    donor
           370. Same donor as current transplant? 1 ☐ Yes   0 ☐ No
                  Yes No   Yes No
           371. 1☐ 0☐ Bone marrow   **374.** 1☐ 0☐ Fetal tissue
           372. 1☐ 0☐ Peripheral blood **375.** 1☐ 0☐ Other, specify: _____
           373. 1☐ 0☐ Cord blood

           376. Was this transplant reported to the IBMTR?
                  1 ☐ Yes ───── IBMTR I.D. ☐☐☐☐☐☐☐
                  0 ☐ No
                  8 ☐ Unknown

3 ☐ **Allogeneic,** ─────
    related donor
           377. Same donor as current transplant? 1 ☐ Yes   0 ☐ No
                  Yes No   Yes No
           378. 1☐ 0☐ Bone marrow   **380.** 1☐ 0☐ Cord blood
           379. 1☐ 0☐ Peripheral blood **381.** 1☐ 0☐ Other, specify: _____

           382. Was this transplant reported to the IBMTR?
                  1 ☐ Yes ───── IBMTR I.D. ☐☐☐☐☐☐☐
                  0 ☐ No
                  8 ☐ Unknown

383. Reason for re-transplant:
    1 ☐ No engraftment   5 ☐ Recurrent malignancy
    2 ☐ Partial engraftment   6 ☐ Planned second transplant, per protocol
    3 ☐ Graft failure/rejection   7 ☐ Other, specify: _____
    4 ☐ Persistent malignancy

384. What type of graft did patient receive for the current transplant?

1 ☐ Autologous ─────
2 ☐ Allogeneic
3 ☐ Syngeneic

    385. From where were stem cells obtained?
        1 ☐ Bone marrow ───────── *Complete INSERT* **AUTOBM**
        2 ☐ Blood ─────────────── *Complete INSERT* **AUTOPB**
        3 ☐ Bone marrow & Blood ── *Complete INSERTS* **AUTOBM & AUTOPB**

Complete INSERT **ALLOBM**

Posttransplant Information

Provide information for first 100 days after transplant __OR__ until start of conditioning (high-dose therapy) for second or subsequent transplant if started < 100 days after initial transplant __OR__ until infusion of cells for second transplant without conditioning if done < 100 days after initial transplant __OR__ until donor leukocyte infusion done to treat relapse, infection, or lymphoproliferative disorder or graft failure if done < 100 days after initial transplant __OR__ until time of death if death occurred < 100 days after transplant. If this form is being completed more than 100 days after transplant, provide data to 100 days on this form. Provide data for course after 100 days on a follow-up form. **IF YOU HAVE ANY QUESTIONS ABOUT HOW TO COMPLETE THIS SECTION OF THE FORM, PLEASE CONTACT THE STATISTICAL CENTER.**

---

386. Date of last actual contact with patient to determine medical status for this report: ☐☐ ☐☐ ☐☐
Month   Day   Year

387. Did patient die prior to day 100 after this transplant?

  1 ☐ Yes – *Answers to subsequent questions should reflect clinical status immediately prior to death*

  0 ☐ No – *Answers to subsequent questions should reflect clinical status on day of actual contact for this follow-up examination (approximately 100 days posttransplant)*

388. Did patient receive a subsequent blood or marrow infusion after the transplant for which this report is being completed? **(other than peripheral blood leukocytes or T-lymphocytes from original allogeneic donor)**

  1 ☐ Yes

  0 ☐ No

Answers to the following questions should reflect clinical status immediately prior to start of conditioning for subsequent infusion. **A separate report covering the subsequent transplant must be submitted.**

389. Date of subsequent infusion: ☐☐ ☐☐ ☐☐
Month   Day   Year

390. Reason for subsequent infusion:

  1 ☐ No engraftment

  2 ☐ Partial engraftment

  3 ☐ Late graft failure

  4 ☐ Persistent malignancy

  5 ☐ Relapse

  6 ☐ Planned second transplant, per protocol

  7 ☐ Other, specify: _____

391. Type of graft:

  1 ☐ Allogeneic, related

  2 ☐ Allogeneic, unrelated

  3 ☐ Autologous

Donor:

  1 ☐ Same donor

  2 ☐ Different donor

  3 ☐ Not applicable, initial transplant was autologous

Source of cells:

392. 1 ☐ Fresh

    2 ☐ Cryopreserved

393. Check all that apply:

  1 ☐ Yes 0 ☐ No Bone marrow

  1 ☐ Yes 0 ☐ No Peripheral blood

  1 ☐ Yes 0 ☐ No Cord blood

  1 ☐ Yes 0 ☐ No Fetal tissue

  1 ☐ Yes 0 ☐ No Other, specify:_____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

395. *Allografts only:* Has patient received an infusion of peripheral blood leukocytes or T-lymphocytes from the original donor?

1 ☐ Yes ———
0 ☐ No

396. Date first infusion given: ☐☐ ☐☐ ☐☐
                               Month Day Year

397. Patient weight within 2 weeks of first infusion: ☐☐ kg

398. Total number of infusions: ☐☐

399. Total dose of mononuclear cells given: ☐☐☐ . ☐ x 10^{10}

400. Were cells manipulated prior to infusion?

   1 ☐ Yes ———
   0 ☐ No

   401. Indicate method:
      1 ☐ T-cell depletion
      2 ☐ CD34 selection
      7 ☐ Other, specify: _____

402. Indication for the infusion(s) of donor cells:

   1 ☐ Prophylaxis against B-cell lymphoproliferative disorder (or viral infection)
   2 ☐ Prophylaxis against relapse

   3 ☐ Treatment of relapse
   4 ☐ Treatment of B-cell lymphoproliferative disorder
   5 ☐ Treatment of viral infection, specify: _____
   6 ☐ Graft failure
   7 ☐ Other, specify: _____

   If answers 3 – 7 were selected, then answers to following questions should reflect clinical status immediately prior to infusion. **This is considered a transplant and a separate report covering this infusion and post-infusion events must be submitted.**

TEAM □□□□ IUBMID □□□□□□

Hematopoietic Reconstitution Posttransplant

403. Has patient received hematopoietic growth factors or cytokines posttransplant?   1 ☐ Yes   0 ☐ No

Specify agents given as <u>planned</u> therapy to promote engraftment:

		Yes	No		Date Started				Date Stopped		
Per Protocol:					Month	Day	Year		Month	Day	Year
G-CSF	404.	1☐	0☐	405.	□	□	□	406.	□	□	□
GM-CSF	407.	1☐	0☐	408.	□	□	□	409.	□	□	□
Interleukin-3	410.	1☐	0☐	411.	□	□	□	412.	□	□	□
Interleukin-6	413.	1☐	0☐	414.	□	□	□	415.	□	□	□
PIXY-321	416.	1☐	0☐	417.	□	□	□	418.	□	□	□
Stem Cell Factor (SCF)	419.	1☐	0☐	420.	□	□	□	421.	□	□	□
Blinded growth factor trial, specify agent(s) being studied:	422.	1☐	0☐	423.	□	□	□	424.	□	□	□
Other, specify:	425.	1☐	0☐	426.	□	□	□	427.	□	□	□

Coding for Indication of Therapy (below)
1. Intervention for delay/decline in Absolute Neutrophil Count (ANC)
2. Intervention for delay/decline in platelets
3. Intervention for delay/decline in both ANC and platelets
4. Intervention for delay/decline in red blood cell counts
5. Anti-leukemic or tumor agent to <u>prevent</u> relapse
6. Anti-leukemic or tumor agent to <u>treat</u> relapse
7. Other indication

Specify additional agents given:

		Yes	No		Date Started				Date Stopped			Indication	
					Month	Day	Year		Month	Day	Year		
G-CSF	428.	1☐	0☐	429.	□	□	□	430.	□	□	□	431.	☐
GM-CSF	432.	1☐	0☐	433.	□	□	□	434.	□	□	□	435.	☐
Erythropoietin	436.	1☐	0☐	437.	□	□	□	438.	□	□	□	439.	☐
Thrombopoietin	440.	1☐	0☐	441.	□	□	□	442.	□	□	□	443.	☐
Interleukin-2	444.	1☐	0☐	445.	□	□	□	446.	□	□	□	447.	☐
Interleukin-3	448.	1☐	0☐	449.	□	□	□	450.	□	□	□	451.	☐
Interleukin-6	452.	1☐	0☐	453.	□	□	□	454.	□	□	□	455.	☐
PIXY-321	456.	1☐	0☐	457.	□	□	□	458.	□	□	□	459.	☐
Stem Cell Factor (SCF)	460.	1☐	0☐	461.	□	□	□	462.	□	□	□	463.	☐
Interferon-alpha	464.	1☐	0☐	465.	□	□	□	466	□	□	□	467.	☐
Interferon-gamma	468.	1☐	0☐	469.	□	□	□	470.	□	□	□	471.	☐
Blinded growth factor trial, specify agent(s) being studied:	472.	1☐	0☐	473.	□	□	□	474.	□	□	□	475.	☐
Other, specify:	476.	1☐	0☐	477.	□	□	□	478.	□	□	□	479.	☐

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐☐

480. Did patient receive other courses of growth factors or cytokines posttransplant?

1 ☐ Yes ── ⌜ *Photocopy Q.428–479 and answer for each additional course given.* ⌝

0 ☐ No

8 ☐ Unknown

Granulopoiesis

481. Is (was) there evidence of hematopoietic recovery following the initial bone marrow infusion? *(check only one)*

1 ☐ Yes, ───
ANC $\geq$ 500/mm³ achieved and sustained for 3 consecutive days

> **482.** Date ANC $\geq$ 500/mm³: *(First of 3 consecutive days)* ☐☐ ☐☐ ☐☐
> Month Day Year
>
> **483.** Was ANC $\geq$ 1000/mm³ achieved and sustained for 3 consecutive days?
>
> 1 ☐ Yes── **484.** Date achieved: ☐☐ ☐☐ ☐☐ ☐ Date unknown
> 0 ☐ No Month Day Year
> 8 ☐ Unknown *(first of 3 consecutive days)*
>
> ⌊ Go to Q. 512 ⌋

2 ☐ Yes, ───
ANC $\geq$ 500/mm³ for 3 consecutive days with subsequent decline in ANC to <500/mm³ for greater than 3 days

> **485.** Date ANC $\geq$ 500/mm³: *(First of 3 consecutive days)* ☐☐ ☐☐ ☐☐
> Month Day Year
>
> **486.** Was ANC $\geq$ 1000/mm³ achieved and sustained for 3 consecutive days?
>
> 1 ☐ Yes── **487.** Date achieved: ☐☐ ☐☐ ☐☐ ☐ Date unknown
> 0 ☐ No Month Day Year
> 8 ☐ Unknown *(first of 3 consecutive days)*
>
> **488.** Date of decline in ANC to < 500/mm³ for greater than 3 days: *(First of 3 days that ANC declined)*
>
> ☐☐ ☐☐ ☐☐
> Month Day Year
>
> **489.** Did patient recover and maintain ANC $\geq$ 500/mm³ following the decline?
>
> 1 ☐ Yes ── **490.** Date of ANC recovery:
> 0 ☐ No ☐☐ ☐☐ ☐☐
> Month Day Year
>
> ⌊ Go to Q. 491 ⌋

3 ☐ No, ANC $\geq$ 500/mm³ was not achieved and there was ────── ⌊ Go to Q. 491 ⌋
no evidence of recurrent disease in the bone marrow

4 ☐ No, ANC $\geq$ 500/mm³ was not achieved and there was documented── ⌊ Go to Q. 491 ⌋
persistent disease in the bone marrow posttransplant

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

Suspected etiology of failure to achieve ANC ≥ 500/mm³ or of a decline in ANC:

491. Persistent disease or relapse:
1 ☐ Yes
0 ☐ No
8 ☐ Unknown

492. Graft versus host disease:
1 ☐ Yes
0 ☐ No
8 ☐ Unknown

493. Immune-mediated rejection:
1 ☐ Yes
0 ☐ No
8 ☐ Unknown

494. Non-viral infection:
1 ☐ Yes
0 ☐ No
8 ☐ Unknown

495. Suspected viral infection:
1 ☐ Yes ————
0 ☐ No
8 ☐ Unknown

Virus suspected:

	Yes	No	
496.	1 ☐	0 ☐	Cytomegalovirus (CMV)
497.	1 ☐	0 ☐	Human Herpes Virus Type 6 (HHV6)
498.	1 ☐	0 ☐	Herpes Simplex Virus (HSV)
499.	1 ☐	0 ☐	Varicella
500.	1 ☐	0 ☐	Other, specify:

_____

501. Documented viral infection:
1 ☐ Yes ————
0 ☐ No
8 ☐ Unknown

Virus involved:

	Yes	No	
502.	1 ☐	0 ☐	Cytomegalovirus (CMV)
503.	1 ☐	0 ☐	Human Herpes Virus Type 6 (HHV6)
504.	1 ☐	0 ☐	Herpes Simplex Virus (HSV)
505.	1 ☐	0 ☐	Varicella
506.	1 ☐	0 ☐	Other, specify:

_____

507. Drugs:
1 ☐ Yes ————
0 ☐ No
8 ☐ Unknown

	Yes	No	
508.	1 ☐	0 ☐	Ganciclovir
509.	1 ☐	0 ☐	Bactrim, Septra, Trimethoprim-sulfamethoxazole
510.	1 ☐	0 ☐	Other, specify:

_____

511. Etiology undetermined:
1 ☐ Yes
0 ☐ No

Megakaryopoiesis

The following questions relate to <u>initial</u> platelet recovery. All dates should reflect no transfusions in previous 7 days, and the first of 3 consecutive laboratory results.

512. Was a platelet count of $\geq 20 \times 10^9$/L achieved?

1 ☐ Yes ──────────────┐
0 ☐ No ──────┐   **513.** Date platelets $\geq 20 \times 10^9$/L: [ ][ ] [ ][ ] [ ][ ]
8 ☐ Unknown─┤ Go to Q. 518 │   ☐ Date unknown   Month Day Year

514. Was a platelet count of $\geq 50 \times 10^9$/L achieved?

1 ☐ Yes ──────────────┐
0 ☐ No ──────┐   **515.** Date platelets $\geq 50 \times 10^9$/L: [ ][ ] [ ][ ] [ ][ ]
8 ☐ Unknown─┤ Go to Q. 518 │   ☐ Date unknown   Month Day Year

516. Was a platelet count of $\geq 100 \times 10^9$/L achieved?

1 ☐ Yes ──────────────┐
0 ☐ No   **517.** Date platelets $\geq 100 \times 10^9$/L: [ ][ ] [ ][ ] [ ][ ]
8 ☐ Unknown   ☐ Date unknown   Month Day Year

518. Was patient ever platelet transfusion independent?

1 ☐ Yes ──────────────┐
0 ☐ No   **519.** Date of last (most recent) platelet transfusion*: [ ][ ] [ ][ ] [ ][ ]
8 ☐ Unknown   ☐ Date unknown   Month Day Year
7 ☐ Not applicable   *If patient was platelet transfusion independent for ≥ 14 days but subsequently experienced a decline in platelet
   (never   count and required platelet transfusions, record date of last platelet transfusion <u>before decline in counts</u>. If patient
   dependent)   has not required platelet transfusions since initial date of recovery, record date of last platelet transfusion.

520. Is patient now receiving platelet transfusions?

1 ☐ Yes
0 ☐ No
8 ☐ Unknown

Erythropoiesis

521. Has patient received red blood cell (RBC) transfusions within 20 days of the day of last contact?

1 ☐ Yes
0 ☐ No ──────┐ **522.** Date of last (most recent) RBC transfusion*: [ ][ ] [ ][ ] [ ][ ]
             ☐ Date unknown   Month Day Year

             *If patient was RBC transfusion independent for ≥ 1 month but subsequently experienced a decline in RBC
             count and required RBC transfusions, record date of last RBC transfusion <u>before decline in counts</u>. If patient
             has not required RBC transfusions since initial date of recovery, record date of last RBC transfusion.

523. Is patient now receiving RBC transfusions?

1 ☐ Yes
0 ☐ No
8 ☐ Unknown

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

Current Hematologic Findings

Date of most recent CBC: ☐☐ ☐☐ ☐☐
                        Month Day Year

Actual CBC results:

WBC: ☐☐☐.☐ x 10⁹/L

Neutrophils: ☐☐ %

Lymphocytes: ☐☐ %

Hemoglobin: ☐☐☐☐.☐☐   ☐ Transfused

Hematocrit: ☐☐ %   ☐ Transfused

Platelets: ☐☐ x 10⁹/L   ☐ Transfused

Specify units for hemoglobin: ☐ g/dL
                              ☐ g/L
                              ☐ mmol/L

Acute Graft-vs-Host Disease (GVHD)

524. Was specific therapy used posttransplant to prevent or induce acute GVHD, or promote engraftment?

1 ☐ Yes

0 ☐ No

8 ☐ Unknown

Allografts:
Go to Q. 541

Autografts:
Go to Q. 680

For each agent listed below indicate whether or not it was used to prevent or induce acute GVHD:

	Yes	No	
525.	1 ☐	0 ☐	Methotrexate
526.	1 ☐	0 ☐	Cyclosporine
527.	1 ☐	0 ☐	FK 506 (Tacrolimus)
528.	1 ☐	0 ☐	Corticosteroids
529.	1 ☐	0 ☐	ALS, ALG, ATS, ATG
530.	1 ☐	0 ☐	Azathioprine
531.	1 ☐	0 ☐	Cyclophosphamide
532.	1 ☐	0 ☐	In vivo anti T-lymphocyte monoclonal antibody

	Yes	No	
533.	1 ☐	0 ☐	Anti IL-2
534.	1 ☐	0 ☐	Anti CD 25
535.	1 ☐	0 ☐	Campath
536.	1 ☐	0 ☐	OKT3
537.	1 ☐	0 ☐	Other, specify: _____

538. 1 ☐ 0 ☐ In vivo immunotoxin, specify: _____

539. 1 ☐ 0 ☐ Blinded randomized trial; specify agent being studied: _____

540. 1 ☐ 0 ☐ Other, specify: _____

TEAM [ ][ ][ ]   IUBMID [ ][ ][ ][ ][ ][ ]

541. Did acute GVHD occur?

   1 ☐ Yes ──────────────────┐

   0 ☐ No ──┐

            │ Go to Q. 593 │

   8 ☐ Unknown ──┘

542. Maximum overall grade: 1 ☐ I   2 ☐ II   3 ☐ III   4 ☐ IV

What was diagnosis based on?

543. Histologic evidence:

   1 ☐ Yes ──────

   0 ☐ No

Sites:			
	Yes	No	
544.	1 ☐	0 ☐	Skin
545.	1 ☐	0 ☐	Gut
546.	1 ☐	0 ☐	Liver
547.	1 ☐	0 ☐	Other, specify:

548. Clinical evidence:

   1 ☐ Yes

   0 ☐ No

549. Date of onset: [ ][ ] [ ][ ] [ ][ ]

             Month   Day   Year

550. Was acute GVHD still present at time of this report?

   1 ☐ Yes

   0 ☐ No

   2 ☐ Progressed to chronic GVHD

   8 ☐ Unknown

List the maximum severity of organ involvement attributed to acute GVHD:

	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
551. Skin:	1 ☐ No rash	2 ☐ Maculopapular rash, <25% of body surface	3 ☐ Maculopapular rash, 25–50% of body surface	4 ☐ Generalized erythroderma	5 ☐ Generalized erythroderma with bullae formation and desquamation

552. Intestinal tract (use ml/day for adult patients and ml/m²/day for pediatric patients):

Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
0 ☐ No diarrhea 1 ☐ Diarrhea ≤500 ml/day or <280 ml/m²/day	2 ☐ Diarrhea >500 but ≤1000 ml/day or 280–555 ml/m²/day	3 ☐ Diarrhea >1000 but ≤1500 ml/day or 556–833 ml/m²/day	4 ☐ Diarrhea >1500 ml/day or >833 ml/m²/day	5 ☐ Severe abdominal pain, with or without ileus

553. Liver:

Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
1 ☐ Bilirubin <2.0 mg/dL	2 ☐ Bilirubin 2.0–3.0 mg/dL	3 ☐ Bilirubin 3.1–6.0 mg/dL	4 ☐ Bilirubin 6.1–15.0 mg/dL	5 ☐ Bilirubin >15.0 mg/dL

554. Other organ involvement?

   1 ☐ Yes ──────

   0 ☐ No

	Yes	No	
555.	1 ☐	0 ☐	Upper GI tract
556.	1 ☐	0 ☐	Lung
557.	1 ☐	0 ☐	Other, specify: _____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

558. Was specific therapy used to **treat** acute GVHD? 1 ☐ Yes   0 ☐ No ─(Go to Q. 593)

For each agent listed below indicate whether or not it was used to **treat** acute GVHD

	No, drug not given	Drug continued at prophylactic dose	Yes, drug started	Yes, dose increased	Still taking? Yes	No
559. Methotrexate	0 ☐	1 ☐	2 ☐	3 ☐	**560.** 1 ☐	0 ☐
561. Cyclosporine	0 ☐	1 ☐	2 ☐	3 ☐	**562.** 1 ☐	0 ☐
563. FK 506 (Tacrolimus)	0 ☐	1 ☐	2 ☐	3 ☐	**564.** 1 ☐	0 ☐
565. Systemic Corticosteroids	0 ☐	1 ☐	2 ☐	3 ☐	**566.** 1 ☐	0 ☐
567. Topical Corticosteroids	0 ☐	1 ☐	2 ☐	3 ☐	**568.** 1 ☐	0 ☐
569. ALS, ALG, ATS, ATG	0 ☐	1 ☐	2 ☐	3 ☐	**570.** 1 ☐	0 ☐
571. Azathioprine	0 ☐	1 ☐	2 ☐	3 ☐	**572.** 1 ☐	0 ☐
573. Cyclo-phosphamide	0 ☐	1 ☐	2 ☐	3 ☐	**574.** 1 ☐	0 ☐
575. Thalidomide	0 ☐	1 ☐	2 ☐	3 ☐	**576.** 1 ☐	0 ☐

In vivo anti-T-lymphocyte monoclonal antibody:

	No, drug not given	Drug continued at prophylactic dose	Yes, drug started	Yes, dose increased	Still taking? Yes	No
577. Anti IL-2	0 ☐	1 ☐	2 ☐	3 ☐	**578.** 1 ☐	0 ☐
579. Anti CD 25	0 ☐	1 ☐	2 ☐	3 ☐	**580.** 1 ☐	0 ☐
581. Campath	0 ☐	1 ☐	2 ☐	3 ☐	**582.** 1 ☐	0 ☐
583. OKT3	0 ☐	1 ☐	2 ☐	3 ☐	**584.** 1 ☐	0 ☐
585. Other, specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**586.** 1 ☐	0 ☐
587. In vivo immunotoxin, specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**588.** 1 ☐	0 ☐
589. Blinded randomized trial; specify agent being studied: _____	0 ☐	1 ☐	2 ☐	3 ☐	**590.** 1 ☐	0 ☐
591. Other, specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**592.** 1 ☐	0 ☐

Chronic Graft-vs-Host Disease (GVHD)

593. Has patient developed clinical chronic GVHD?

1 ☐ Yes ─────────────────────────┐

0 ☐ No ──────┐ ┌─────────┐   │

8 ☐ Unknown──┤ │ Go to   │   │
             └─┤ Q. 680 │   │
               └─────────┘   │

594. Date of onset: ☐☐ ☐☐ ☐☐ ──── **595.** Progressed from acute GVHD?

Month Day Year

                      1 ☐ Yes

                      0 ☐ No

596. Karnofsky/Lansky score (see page 5) at diagnosis of chronic GVHD: ☐☐☐

597. Platelet count at diagnosis of chronic GVHD: ☐☐☐☐☐ . ☐ x 10^9/L

598. Total serum bilirubin at diagnosis of chronic GVHD: ☐☐ . ☐

599. Unit of measurement for bilirubin:

    1 ☐ mg/dL

    2 ☐ μmol/L

What was diagnosis based on?

600. Histologic evidence:

    1 ☐ Yes

    0 ☐ No

609. Clinical evidence:

    1 ☐ Yes

    0 ☐ No

Sites:

	Yes	No	
601.	1 ☐	0 ☐	Skin
602.	1 ☐	0 ☐	Gut
603.	1 ☐	0 ☐	Liver
604.	1 ☐	0 ☐	Buccal mucosa/lip
605.	1 ☐	0 ☐	Conjunctiva
606.	1 ☐	0 ☐	Lung
607.	1 ☐	0 ☐	Muscle
608.	1 ☐	0 ☐	Other, specify:

610. Maximum grade of chronic GVHD:

    1 ☐ Limited (*Localized skin involvement and/or hepatic dysfunction due to chronic GVHD*)

    2 ☐ Extensive (*Generalized skin involvement; or localized skin involvement and/or hepatic dysfunction due to chronic GVHD, plus :*
        -Liver histology showing chronic aggressive hepatitis, bridging necrosis or cirrhosis; or,
        -Involvement of eye: Schirmer's test with < 5 mm wetting; or,
        -Involvement of minor salivary glands or oral mucosa demonstrated on labial biopsy; or,
        -Involvement of any other target organ)

611. Overall severity: 1 ☐ Mild   2 ☐ Moderate   3 ☐ Severe

Continued on next page

Indicate organ involvement with chronic GVHD from list below:

		Yes	No	
Skin/Hair:	612.	1 ☐	0 ☐	Subclinical (biopsy findings only)
	613.	1 ☐	0 ☐	Rash
	614.	1 ☐	0 ☐	Scleroderma
	615.	1 ☐	0 ☐	Dyspigmentation
	616.	1 ☐	0 ☐	Contractures
	617.	1 ☐	0 ☐	Alopecia
	618.	1 ☐	0 ☐	Other skin/hair involvement, specify: _____
Eyes:	619.	1 ☐	0 ☐	Dry eyes
	620.	1 ☐	0 ☐	Corneal erosion/conjunctivitis
	621.	1 ☐	0 ☐	Other eye involvement, specify: _____
Mouth:	622.	1 ☐	0 ☐	Lichenoid changes
	623.	1 ☐	0 ☐	Mucositis/ulcers
	624.	1 ☐	0 ☐	Other mouth involvement, specify: _____
Lung:	625.	1 ☐	0 ☐	Bronchiolitis obliterans
	626.	1 ☐	0 ☐	Other lung involvement, specify: _____
GI Tract:	627.	1 ☐	0 ☐	Esophageal involvement
	628.	1 ☐	0 ☐	Chronic nausea/vomiting
	629.	1 ☐	0 ☐	Chronic diarrhea
	630.	1 ☐	0 ☐	Malabsorption
	631.	1 ☐	0 ☐	Other GI tract involvement, specify: _____
Liver:	632.	1 ☐	0 ☐	Liver involvement, specify: _____
GU Tract:	633.	1 ☐	0 ☐	Vaginitis/stricture
	634.	1 ☐	0 ☐	Other GU involvement, specify: _____
Musculoskeletal:	635.	1 ☐	0 ☐	Arthritis
	636.	1 ☐	0 ☐	Myositis
	637.	1 ☐	0 ☐	Myasthenia
	638.	1 ☐	0 ☐	Other musculoskeletal involvement, specify: _____
Hematologic:	639.	1 ☐	0 ☐	Thrombocytopenia
	640.	1 ☐	0 ☐	Eosinophilia
	641.	1 ☐	0 ☐	Autoantibodies
	642.	1 ☐	0 ☐	Other hematologic involvement, specify: _____
Other:	643.	1 ☐	0 ☐	Specify: _____

644. Was specific therapy used to **treat** chronic GVHD? 1 ☐ Yes   0 ☐ No ──[Go to Q. 679]

For each agent listed below indicate whether or not it was used to **treat** chronic GVHD

	No, drug not given	Drug continued at prophylactic dose	Yes, drug started	Yes, dose increased	Still taking? Yes	No

645. ALS, ALG, ATS, ATG   0 ☐   [1 ☐   2 ☐   3 ☐]──[**646.** 1 ☐   0 ☐]

647. Azathioprine   0 ☐   [1 ☐   2 ☐   3 ☐]──[**648.** 1 ☐   0 ☐]

649. Cyclosporine   0 ☐   [1 ☐   2 ☐   3 ☐]──[**650.** 1 ☐   0 ☐]

651. FK 506 (Tacrolimus)   0 ☐   [1 ☐   2 ☐   3 ☐]──[**652.** 1 ☐   0 ☐]

653. Systemic Corticosteroids   0 ☐   [1 ☐   2 ☐   3 ☐]──[**654.** 1 ☐   0 ☐]

655. Topical Corticosteroids   0 ☐   [1 ☐   2 ☐   3 ☐]──[**656.** 1 ☐   0 ☐]

657. Cyclo-phosphamide   0 ☐   [1 ☐   2 ☐   3 ☐]──[**658.** 1 ☐   0 ☐]

659. Thalidomide   0 ☐   [1 ☐   2 ☐   3 ☐]──[**660.** 1 ☐   0 ☐]

In vivo anti-T-lymphocyte monoclonal antibody

661. Anti IL-2   0 ☐   [1 ☐   2 ☐   3 ☐]──[**662.** 1 ☐   0 ☐]

663. Anti CD 25   0 ☐   [1 ☐   2 ☐   3 ☐]──[**664.** 1 ☐   0 ☐]

665. Campath   0 ☐   [1 ☐   2 ☐   3 ☐]──[**666.** 1 ☐   0 ☐]

667. OKT3   0 ☐   [1 ☐   2 ☐   3 ☐]──[**668.** 1 ☐   0 ☐]

669. Other, specify: _____   0 ☐   [1 ☐   2 ☐   3 ☐]──[**670.** 1 ☐   0 ☐]

671. In vivo immunotoxin, specify: _____   0 ☐   [1 ☐   2 ☐   3 ☐]──[**672.** 1 ☐   0 ☐]

673. Blinded randomized trial; specify agent being studied: _____   0 ☐   [1 ☐   2 ☐   3 ☐]──[**674.** 1 ☐   0 ☐]

675. Other, specify: _____   0 ☐   [1 ☐   2 ☐   3 ☐]──[**676.** 1 ☐   0 ☐]

677. Is patient still receiving treatment for chronic GVHD?

   1 ☐ Yes

   0 ☐ No———

        678. Date last treatment was administered: ☐☐ ☐☐ ☐☐

                                            Month Day Year

679. Is chronic GVHD still present?

   1 ☐ Yes

   0 ☐ No

   2 ☐ No symptoms, but patient still receiving treatment

Other Treatment and Clinical Status After Start of Conditioning

680. Were transfusions given at any time after the start of conditioning to present?

   1 ☐ Yes———

   0 ☐ No

	Yes	No	
681.	1 ☐	0 ☐	Did patient receive only CMV-negative blood products?
682.	1 ☐	0 ☐	Were blood products filtered to remove leukocytes?
683.	1 ☐	0 ☐	Were all transfusions irradiated?

684. Number of RBC transfusions in first 60 days: ☐☐☐ units

685. Number of platelet transfusions in first 60 days: ☐☐☐ units

686. Did patient receive any of the following agents for infection <u>prophylaxis</u> after start of conditioning?

   1 ☐ Yes———

   0 ☐ No

	Yes	No	
	1 ☐	0 ☐	Systemic antibacterial antibiotics
	1 ☐	0 ☐	Nonabsorbable antibiotics
687.	1 ☐	0 ☐	Polyclonal IV gamma globulin (not ATG)
688.	1 ☐	0 ☐	CMV/hyperimmune gamma globulin
689.	1 ☐	0 ☐	IV amphotericin
690.	1 ☐	0 ☐	Fluconazole
691.	1 ☐	0 ☐	Itraconazole
692.	1 ☐	0 ☐	Other systemic antifungal agent, specify:_____
693.	1 ☐	0 ☐	Acyclovir
694.	1 ☐	0 ☐	Ganciclovir (DHPG)
695.	1 ☐	0 ☐	Foscarnet
696.	1 ☐	0 ☐	Other antiviral agent, specify: _____
697.	1 ☐	0 ☐	Trimethoprim-sulfamethoxazole (Bactrim/Septra)
698.	1 ☐	0 ☐	Pentamidine inhaled
699.	1 ☐	0 ☐	Pentamidine IV
700.	1 ☐	0 ☐	Dapsone
701.	1 ☐	0 ☐	Other pneumocystis prophylaxis, specify:_____
702.	1 ☐	0 ☐	Other, specify:_____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

703. Did patient develop clinically significant infection after start of conditioning?   1 ☐ Yes   0 ☐ No

---

Select site and organism from lists shown on the next page and place number in the appropriate spaces. If more than one site or organism was involved, list one site of infection and organism on the first line; second site and/or organism on second line.

				Date of Onset			Did infection resolve?	
		Site	Organism	Month	Day	Year	Yes	No

704. ☐ Bacterial

Typical First   **705.** ☐☐   **706.** _____   **707.** ☐☐ ☐☐ ☐☐   **708.** 1 ☐ 0 ☐

Second **709.** ☐☐   **710.** _____   **711.** ☐☐ ☐☐ ☐☐   **712.** 1 ☐ 0 ☐

Atypical First   **716.** ☐☐   **717.** B☐☐☐   **718.** ☐☐ ☐☐ ☐☐   **719.** 1 ☐ 0 ☐

Second **720.** ☐☐   **721.** B☐☐☐   **722.** ☐☐ ☐☐ ☐☐   **723.** 1 ☐ 0 ☐

724. Other atypical bacterium, specify: _____

727. ☐ Fungal

First   **728.** ☐☐   **729.** F☐☐☐   **730.** ☐☐ ☐☐ ☐☐   **731.** 1 ☐ 0 ☐

Second **732.** ☐☐   **733.** F☐☐☐   **734.** ☐☐ ☐☐ ☐☐   **735.** 1 ☐ 0 ☐

736. Other fungus, specify: _____

739. ☐ Viral

First   **740.** ☐☐   **741.** V☐☐☐   **742.** ☐☐ ☐☐ ☐☐   **743.** 1 ☐ 0 ☐

Second **744.** ☐☐   **745.** V☐☐☐   **746.** ☐☐ ☐☐ ☐☐   **747.** 1 ☐ 0 ☐

748. Other virus, specify: _____

751. ☐ Parasitic

First   **752.** ☐☐   **753.** P☐☐☐   **754.** ☐☐ ☐☐ ☐☐   **755.** 1 ☐ 0 ☐

Second **756.** ☐☐   **757.** P☐☐☐   **758.** ☐☐ ☐☐ ☐☐   **759.** 1 ☐ 0 ☐

760. Other parasite, specify: _____

763. ☐ No organism identified

First   **764.** ☐☐   **765.** O 5 0 9   **766.** ☐☐ ☐☐ ☐☐   **767.** 1 ☐ 0 ☐

Second **768.** ☐☐   **769.** O 5 0 9   **770.** ☐☐ ☐☐ ☐☐   **771.** 1 ☐ 0 ☐

Codes for Common Sites of Infection

01	Blood / buffy coat	40	*Genito-Urinary Tract unspecified*
02	Disseminated – generalized, isolated at 3 or more distinct sites	41	Kidneys, renal pelvis, ureters and bladder
		42	Prostate
03	*Central Nervous System unspecified*	43	Testes
04	Brain	44	Fallopian tubes, uterus, cervix
05	Spinal cord	45	Vagina
06	Meninges and CSF	50	*Skin unspecified*
10	*Gastrointestinal Tract unspecified*	51	Genital area
11	Lips	52	Cellulitis
12	Tongue, oral cavity and oro-pharynx	53	Herpes Zoster
13	Esophagus	54	Rash, pustules or abscesses not typical of any of the above
14	Stomach		
15	Gallbladder and biliary tree (not hepatitis), pancreas	60	Central venous catheter, not otherwise specified
16	Small intestine	61	Catheter insertion site
17	Large intestine	62	Catheter tip
18	Feces/stool	70	Eyes
19	Peritoneum	75	Ear
20	Liver	80	*Other unspecified*
30	*Respiratory unspecified*	81	Joints
31	Upper airway and nasopharynx	82	Bone marrow
32	Laryngitis/larynx	83	Bone cortex (osteomyelitis)
33	Lower respiratory tract (lung)	84	Muscle (excluding cardiac)
34	Pleural cavity, pleural fluid	85	Cardiac (endocardium, myocardium, pericardium)
35	Sinuses	86	Lymph nodes
		87	Spleen

Codes for Commonly Reported Organisms

1. Bacteria
(Indicate code for atypical bacteria; list bacterium for non-atypical bacteria.)

100	Atypical bacteria, not otherwise specified
101	Coxiella
102	Legionella
103	Leptospira
104	Listeria
105	Mycoplasma
106	Nocardia
107	Rickettsia
110	Tuberculosis, NOS (AFB, acid fast bacillus, Koch bacillus)
111	Typical tuberculosis (TB, Tuberculosis)
112	Mycobacteria (avium, bovium, intracellulare)
113	Chlamydia
119	Other atypical bacteria, specify

2. Fungal Infections
200	Candida, not otherwise specified
201	Candida albicans
202	Candida krusei
203	Candida parapsilosis
204	Candida tropicalis
205	Torulopsis glabrata (a subspecies of candida)
209	Candida, other
210	Aspergillus, not otherwise specified
211	Aspergillus flavus
212	Aspergillus fumigatus
213	Aspergillus niger
219	Aspergillus, other
220	Cryptococcus species
230	Fusarium species
240	Mucormycosis (zygomycetes, rhizopus)
250	Yeast, not otherwise specified
259	Other fungus, specify

3. Viral Infections
301	Herpes Simplex (HSV1, HSV2)
302	Herpes Zoster (Chicken pox, Varicella)
303	Cytomegalovirus (CMV)
304	Adenovirus
305	Enterovirus (Coxsackie, Echo, Polio)
306	Hepatitis A (HAV)
307	Hepatitis B (HBV, Australian antigen)
308	Hepatitis C (HCV)
309	HIV-1 (HTLV-III)
310	Influenza
311	Measles (Rubeola)
312	Mumps
313	Papovavirus
314	Respiratory syncytial virus (RSV)
315	Rubella (German Measles)
316	Parainfluenza
317	Human herpesvirus-6 (HHV-6)
318	Epstein-Barr virus (EBV)
319	Polyomavirus
320	Rotavirus
321	Rhinovirus
329	Other viral, specify

4. Parasite Infections
401	Pneumocystis (PCP)
402	Toxoplasma
403	Giardia
404	Cryptosporidium
409	Other parasite (amebiasis, echinococcal cyst, trichomonas – either vaginal or gingivitis), specify

5. Other Infections
509	No organism identified

Pulmonary function

775. Has patient developed interstitial pneumonitis (IPn)?

> *Interstitial pneumonitis is characterized by hypoxia and diffuse interstitial infiltrates on chest x-ray not caused by fluid overload.*

1 ☐ Yes
0 ☐ No

776. How many episodes of IPn occurred? ☐

> *Note: If more than one episode of IPn, photocopy this page and complete Q. 775 – 795 for subsequent episode(s).*

777. Date of onset of IPn: ☐☐ ☐☐ ☐☐
                              Month   Day   Year

778. Were diagnostic tests other than radiographic studies done?

1 ☐ Yes
0 ☐ No

> Diagnosis was evaluated by:
>
> | | Yes | No | |
> |---|---|---|---|
> | **779.** | 1 ☐ | 0 ☐ | Bronchoalveolar lavage |
> | **780.** | 1 ☐ | 0 ☐ | Transbronchial biopsy |
> | **781.** | 1 ☐ | 0 ☐ | Open lung biopsy |
> | **782.** | 1 ☐ | 0 ☐ | Autopsy |
> | **783.** | 1 ☐ | 0 ☐ | Other, specify: _____ |

784. Was an organism isolated?

1 ☐ Yes
0 ☐ No (idiopathic, or no organism isolated)

> Etiology:
>
> | | Yes | No | |
> |---|---|---|---|
> | **785.** | 1 ☐ | 0 ☐ | Pneumocystis carinii |
> | **786.** | 1 ☐ | 0 ☐ | Aspergillus |
> | **787.** | 1 ☐ | 0 ☐ | Candida toxoplasma |
> | **788.** | 1 ☐ | 0 ☐ | Respiratory syncytial virus |
> | **789.** | 1 ☐ | 0 ☐ | Cytomegalovirus |
> | **790.** | 1 ☐ | 0 ☐ | Herpes simplex |
> | **791.** | 1 ☐ | 0 ☐ | Adenovirus |
> | **792.** | 1 ☐ | 0 ☐ | Human herpes virus 6 |
> | **793.** | 1 ☐ | 0 ☐ | Other virus, specify: _____ |
> | **794.** | 1 ☐ | 0 ☐ | Other, specify: _____ |

795. Has interstitial pneumonitis resolved?

1 ☐ Yes
0 ☐ No
8 ☐ Unknown

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐ .

796. Did patient develop pulmonary abnormalities other than interstitial pneumonitis <u>after start of conditioning</u>?

1 ☐ Yes

0 ☐ No

797. Did patient develop Acute Respiratory Distress Syndrome (ARDS)?

1 ☐ Yes

0 ☐ No

798. Date of onset of ARDS: ☐☐ ☐☐ ☐☐
Month   Day   Year

799. Were diagnostic tests done?

1 ☐ Yes

0 ☐ No

Diagnosis was evaluated by:

	Yes	No	
800.	1 ☐	0 ☐	Bronchoalveolar lavage
801.	1 ☐	0 ☐	Transbronchial biopsy
802.	1 ☐	0 ☐	Open lung biopsy
803.	1 ☐	0 ☐	Autopsy
804.	1 ☐	0 ☐	Other, specify: _____

805. Did patient develop bronchiolitis obliterans?

1 ☐ Yes

0 ☐ No

806. Date of onset: ☐☐ ☐☐ ☐☐
Month   Day   Year

807. Were diagnostic tests done?

1 ☐ Yes

0 ☐ No

Diagnosis was evaluated by:

	Yes	No	
808.	1 ☐	0 ☐	Bronchoalveolar lavage
809.	1 ☐	0 ☐	Transbronchial biopsy
810.	1 ☐	0 ☐	Open lung biopsy
811.	1 ☐	0 ☐	Autopsy
812.	1 ☐	0 ☐	Other, specify: _____

813. Did patient develop pulmonary hemorrhage?

1 ☐ Yes

0 ☐ No

814. Date of onset: ☐☐ ☐☐ ☐☐
Month   Day   Year

815. Were diagnostic tests done?

1 ☐ Yes

0 ☐ No

Diagnosis was evaluated by:

	Yes	No	
816.	1 ☐	0 ☐	Bronchoalveolar lavage
817.	1 ☐	0 ☐	Transbronchial biopsy
818.	1 ☐	0 ☐	Open lung biopsy
819.	1 ☐	0 ☐	Autopsy
820.	1 ☐	0 ☐	Other, specify: _____

821. Did patient develop other non-infectious pulmonary abnormalities?

1 ☐ Yes

0 ☐ No

822. Specify: _____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐ .

Liver function

823. Patient's maximum total bilirubin
in the first 100 days posttransplant: ☐☐ . ☐

> **824.** Unit of measurement for bilirubin:
> • 1 ☐ mg/dL   2 ☐ μmol/L

825. Date of maximum total bilirubin
in the first 100 days posttransplant: ☐☐ ☐☐ ☐☐
Month Day Year

826. Patient's bilirubin on day of last contact: ☐☐ . ☐
(*Refer to Q. 386, page 17 for date*)

> **827.** Unit of measurement for bilirubin:
> 1 ☐ mg/dL   2 ☐ μmol/L

828. Did patient develop any of the following clinical signs/symptoms of abnormal liver function?

1 ☐ Yes
0 ☐ No

>   Yes No
> **829.** 1 ☐ 0 ☐ Jaundice
> **830.** 1 ☐ 0 ☐ Hepatomegaly
> **831.** 1 ☐ 0 ☐ Right upper quadrant pain
> **832.** 1 ☐ 0 ☐ Ascites
> **833.** 1 ☐ 0 ☐ Weight gain (>5%)
> **834.** 1 ☐ 0 ☐ Other, specify:_____

835. Did patient develop non-infectious liver toxicity after conditioning?

1 ☐ Yes
0 ☐ No

> **836.** What was the date of onset? ☐☐ ☐☐ ☐☐
>   Month Day Year
>
> Etiology:
>
>   Yes No
> **837.** 1 ☐ 0 ☐ Veno-occlusive disease
> **838.** 1 ☐ 0 ☐ Other, specify:_____
> **839.** 1 ☐ 0 ☐ Unknown
>
> Diagnosis was based on:
>
>   Yes No
> **840.** 1 ☐ 0 ☐ Clinical signs and symptoms (*see Q. 828*)
> **841.** 1 ☐ 0 ☐ Elevated liver enzymes
> **842.** 1 ☐ 0 ☐ Biopsy
> **843.** 1 ☐ 0 ☐ Autopsy
> **844.** 1 ☐ 0 ☐ Ultrasonography
> **845.** 1 ☐ 0 ☐ Doppler
> **846.** 1 ☐ 0 ☐ Other, specify:_____
>
> **847.** Has liver toxicity resolved?
>
>   1 ☐ Yes
>   0 ☐ No

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

848. Did patient develop any other non-infectious clinically significant organ impairment or disorder after conditioning?

1 ☐ Yes ——

0 ☐ No

	Yes	No	
849.	1☐	0☐	Renal failure requiring dialysis
850.	1☐	0☐	TTP/HUS or similar syndrome
851.	1☐	0☐	Hemorrhage, specify site:

	Yes	No	
852.	1☐	0☐	CNS
853.	1☐	0☐	Upper GI tract
854.	1☐	0☐	Lower GI tract
855.	1☐	0☐	Other, specify: _____

	Yes	No	
856.	1☐	0☐	Hemorrhagic cystitis
857.	1☐	0☐	Seizures
858.	1☐	0☐	Cataracts
859.	1☐	0☐	Avascular necrosis
860.	1☐	0☐	Hypothyroidism
861.	1☐	0☐	Gonadal dysfunction
862.	1☐	0☐	Growth hormone deficiency/growth disturbance
863.	1☐	0☐	Other, specify: _____

864. Did a <u>new</u> malignancy, lymphoproliferative or myeloproliferative disorder appear? *(If more than one new malignancy developed, copy this page and complete for each new cancer)*

1 ☐ Yes ——

0 ☐ No

865. Date of diagnosis: ☐☐ ☐☐ ☐☐
Month Day Year

866. Origin of cells:
1 ☐ Host   8 ☐ Unknown
2 ☐ Donor   7 ☐ Not tested

Diagnosis *(send copy of pathology report/other documentation)*:

	Yes	No	
867.	1☐	0☐	Clonal cytogenetic abnormality without leukemia or MDS
868.	1☐	0☐	Acute myeloid leukemia
869.	1☐	0☐	Other leukemia, specify: _____
870.	1☐	0☐	Myelodysplasia
871.	1☐	0☐	Lymphoma or lymphoproliferative disease

872. EBV positive? 1 ☐ Yes   0 ☐ No   8 ☐ Unknown

	Yes	No	
873.	1☐	0☐	Hodgkin disease
875.	1☐	0☐	Other cancer

876. Primary site: _____

877. Histologic type: _____

878. Behavior:
1 ☐ Benign
2 ☐ In situ
3 ☐ Malignant/invasive
8 ☐ Unknown

Survival and Functional Status

879. Was patient discharged from hospital after transplant?

1 ☐ Yes ————┐

0 ☐ No

7 ☐ Not applicable,
high-dose therapy given as outpatient

880. Date of first discharge from hospital after transplant: ☐☐ ☐☐ ☐☐
Month Day Year

881. **Autografts only:** Total number inpatient days in first 60 days after start of high-dose therapy: ☐☐

882. **Allografts only:** Total number inpatient days in first 100 days after start of high-dose therapy: ☐☐☐

883. Was patient alive on the day of last contact? (*Refer to Q. 386, page 17 for date*):

1 ☐ Yes ————┐

0 ☐ No

┃ Go to Q. 895 ┃

884. *If the patient is 16 years of age or older, complete the Karnofsky Scale.*
If the patient is younger than 16 years of age, complete the Lansky Scale.

Karnofsky Scale (age ≥16 yrs)

Select the phrase in the Karnofsky Scale which best describes the activity status of the patient:

Able to carry on normal activity; no special care is needed.
☐100 Normal; no complaints; no evidence of disease
☐ 90 Able to carry on normal activity
☐ 80 Normal activity with effort

Unable to work; able to live at home, care for most personal needs; a varying amount of assistance is needed.
☐ 70 Cares for self; unable to carry on normal activity or to do active work
☐ 60 Requires occasional assistance but is able to care for most needs
☐ 50 Requires considerable assistance and frequent medical care

Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.
☐ 40 Disabled; requires special care and assistance
☐ 30 Severely disabled; hospitalization indicated, although death not imminent
☐ 20 Very sick; hospitalization necessary
☐ 10 Moribund; fatal process progressing rapidly

Lansky Scale (age <16 yrs)

Select the phrase in the Lansky Play-Performance Scale which best describes the activity status of the patient:

Normal range.
☐100 Fully active
☐ 90 Minor restriction in physically strenuous play
☐ 80 Restricted in strenuous play, tires more easily, otherwise active

Mild to moderate restriction.
☐ 70 Both greater restrictions of, and less time spent in, active play
☐ 60 Ambulatory up to 50% of time, limited active play with assistance/supervision
☐ 50 Considerable assistance required for any active play; fully able to engage in quiet play

Moderate to severe restriction.
☐ 40 Able to initiate quiet activities
☐ 30 Needs considerable assistance for quiet activity
☐ 20 Limited to very passive activity initiated by others (i.e., TV)
☐ 10 Completely disabled, not even passive play

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐☐

(If patient is alive, answer Q.885–894; if dead, skip to Q. 895)

885. Patient (age ≥ 6 years) currently attends school:

1 ☐ Yes ── | **886.** 1 ☐ Part-time   2 ☐ Full-time   8 ☐ Unknown, whether part-time or full-time
0 ☐ No |
| **887.** Date returned to school: ☐☐ ☐☐
| Month   Year

888. Patient was employed outside the home prior to current illness:

1 ☐ Yes ──── | **889.** Patient has returned to work:
0 ☐ No |
| 1 ☐ Yes ── | **890.** Date returned to work: ☐☐ ☐☐
| 0 ☐ No | Month   Year
| |
| | **891.** Patient able to work but is not employed:
| | 1 ☐ Yes
| | 0 ☐ No

| **892.** Patient has resumed all household activities:
| 1 ☐ Yes ── | **893.** Date resumed ☐☐ ☐☐
| 0 ☐ No | all activities: Month   Year
|
| **894.** Patient is a student:
| 1 ☐ Yes
| 0 ☐ No

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐☐

Death Information

895. Date of death: ☐☐ · ☐☐ ☐☐
Month   Day   Year

Cause(s) of death:

Enter appropriate cause of death below. If a code number for "Other, specify" is entered, write the cause in the space provided.	**Cause of Death Codes**
	10 Graft rejection or failure
896. Primary: ☐☐☐ Specify: _____	Infection (other than interstitial pneumonia) 20 Infection, organism not identified 21 Bacterial 22 Fungal 23 Viral 24 Protozoal 29 Other infection, specify
Contributing or secondary causes: **897.** ☐☐☐ Specify: _____	
898. ☐☐☐ Specify: _____	Interstitial pneumonia 30 IPn, idiopathic 31 Cytomegalovirus (CMV) 32 Viral, other 33 Pneumocystis (PCP) 34 Fungal 39 Other IPn, specify
899. ☐☐☐ Specify: _____	
900. ☐☐☐ Specify: _____	
901. ☐☐☐ Specify: _____	40 Adult Respiratory Distress Syndrome, ARDS (other than IPN)
	50 Acute GVHD 60 Chronic GVHD
	70 Recurrence or persistence of primary disease *NOTE: Code "70" may only be used as a primary cause of death, not a contributing or secondary cause.*
	Organ failure (not due to GVHD or infection) 80 Organ failure, not otherwise specified 81 Liver (not VOD) 82 VOD 83 Cardiac (Cardiomyopathy) 84 Pulmonary 85 CNS 86 Renal 89 Other organ failure, specify
	90 Secondary malignancy
	100 Hemorrhage
	110 Accidental death
	900 Other, specify

902. Was cause of death confirmed by autopsy?

1 ☐ Yes ———┐
0 ☐ No   │ **Send copy of autopsy report when available**
8 ☐ Unknown │
6 ☐ Pending ─┘

Confidential/Socioeconomic Information

903. Patient's First Name: ☐☐☐☐☐☐☐☐☐☐

904. Patient's Last Name: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

905. Patient's state of residence (*US only*): ☐☐

906. Zip code for place of patient's <u>residence</u> (*US only*): ☐☐☐☐☐ – ☐☐☐☐

907. Country of residence (*if non-US*): ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

908. Does patient have a US Social Security Number or Canadian Social Insurance Number?

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown
- 7 ☐ Not applicable

909. Social Security or Social Insurance Number: ☐☐☐☐☐☐☐☐☐☐

910. (*For patients ≥18 years of age*) What is patient's marital status? (*check one*)

- 1 ☐ Single, never married
- 2 ☐ Married
- 3 ☐ Separated
- 4 ☐ Divorced
- 5 ☐ Widowed
- 8 ☐ Unknown

911. (*For patients ≥18 years of age*) What is the highest grade patient finished in school?

- 1 ☐ 1 – 8 grades
- 2 ☐ 9 – 11 grades
- 3 ☐ High School graduate
- 4 ☐ Some college
- 5 ☐ Junior college degree
- 6 ☐ College degree (BA/BS)
- 7 ☐ Some post-college work
- 8 ☐ Advanced degree
- 88 ☐ Unknown

912. What type of health insurance does patient have? (*check all that apply*)

- 0 ☐ No Insurance
- 1 ☐ Medicaid
- 2 ☐ Medicare (US)
- 3 ☐ Disability Insurance
- 4 ☐ HMO
- 5 ☐ Individual Health Insurance
- 6 ☐ Group Health Insurance
- 7 ☐ National Health Insurance (non-US)
- 8 ☐ V.A./Military
- 9 ☐ Other, specify:_____

913. (*U.S. patients only*) Type of fee reimbursement:

- 1 ☐ Fee for service
- 2 ☐ Capitation
- 7 ☐ Other, specify: _____
- 8 ☐ Unknown

914. Which category best describes patient's occupation?
If not currently employed, which best describes patient's LAST job? (check only one)

- 1 ☐ Professional, Technical, & Related Occupations (teacher/professor, nurse, lawyer, physician or engineer)
- 2 ☐ Manager, Administrator or Proprietor (sales manager, real estate agent, or postmaster)
- 3 ☐ Clerical & Related Occupations (secretary, clerk, or mail carrier)
- 4 ☐ Sales Occupation (salesperson, demonstrator, agent or broker)
- 5 ☐ Service Occupation (police, cook or hairdresser)
- 6 ☐ Skilled crafts & Related Occupations (carpenter, repairer or telephone line worker)
- 7 ☐ Equipment or Vehicle Operator & Related Occupations (driver, railroad brakeman, or sewer worker)
- 8 ☐ Laborer (helper, longshoreman or warehouse worker)
- 9 ☐ Farmer (owner, manager, operator, or tenant)
- 10 ☐ Member of the military
- 11 ☐ Homemaker
- 90 ☐ Other, please describe: _____
- 88 ☐ Unknown

915. (*US patients only*) What is patient's yearly income, earned by <u>all</u> family members living in household, <u>before taxes</u>? (*check one*)

- 1 ☐ Less than $5,000
- 2 ☐ $ 5,000 – $9,999
- 3 ☐ $10,000 – $19,999
- 4 ☐ $20,000 – $29,999
- 5 ☐ $30,000 – $39,999
- 6 ☐ $40,000 – $49,999
- 7 ☐ $50,000 – $59,999
- 8 ☐ $60,000 – $79,999
- 9 ☐ $80,000 and over
- 88 ☐ Unknown

INSTITUTIONAL INFORMATION

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

(Institutional Unique Blood or Marrow Transplant Identification Number)

Date of transplant for which this form is being completed: ☐☐ ☐☐ ☐☐
Month   Day   Year

Registry: IBMTR   ABMTR   (circle one)

Date of report: ☐☐ ☐☐ ☐☐
Month   Day   Year

1. Signed: _____ / _____
   Person completing this form / Please print name

2. Date form completed: ☐☐ ☐☐ ☐☐
   Month   Day   Year

3. Name of doctor for correspondence: _____

   Institution: _____

   Address: _____

   _____

   _____

   _____

   Telephone: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

   Extension: ☐☐☐ · ☐☐

   Fax: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

4. Make reimbursement check payable to: _____

5. Patient or authorized family member/guardian is aware of, and has consented to, the fact that this case is being entered into the Registry database:

   _____ (physician's initials).

6. A complete report of transplant consists of the following three forms.
   Check when complete:
   - ☐ A (white) CORE FORM
   - ☐ An appropriate (blue or pink) graft-specific insert (Insert ALLOBM, AUTOPB, or AUTOBM)
   - ☐ An appropriate (ivory) disease-specific insert (Inserts I through XVI)

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

(Institutional Unique Blood or Marrow Transplant Identification Number)

Date of transplant for which this form is being completed: ☐☐ ☐☐ ☐☐
Month   Day   Year

Date of report: ☐☐ ☐☐ ☐☐
Month   Day   Year

IBMTR
International Bone Marrow Transplant Registry

IBMTR/ABMTR

Series 095 Reporting Forms

ABMTR
North America
Autologous Blood & Marrow Transplant Registry

Follow-up Information

For living patients, <u>submit follow-up data every 12 months from date of transplant</u>. If patient died since last report, indicate findings present at time of death. For patients lost to follow-up since last report, submit last known information. If another transplant was done since last report, provide information only until date of conditioning for subsequent transplant. If patient received peripheral blood leukocytes from original allogeneic donor since last report to <u>treat</u> relapse, lymphoproliferative disorder, viral infection or graft failure, provide information only until date of infusion (see Q. 33 of this report).

1. Date of last report: ☐☐ ☐☐ ☐☐
Month   Day   Year

2. Patient birthdate: ☐☐ ☐☐ ☐☐
Month   Day   Year

3. Date of last actual contact with patient to determine medical status for this report: ☐☐ ☐☐ ☐☐
Month   Day   Year

Survival and Functional Status

4. Was patient alive on the day of last contact?

1 ☐ Yes

0 ☐ No ——— Go to Q. 15

5. *If the patient is 16 years of age or older, complete the Karnofsky Scale. If the patient is younger than 16 years of age, complete the Lansky Scale.*

Karnofsky Scale (age ≥16 yrs)
Select phrase which best describes activity status:

Able to carry on normal activity; no special care is needed.
☐ 100 Normal; no complaints; no evidence of disease
☐ 90 Able to carry on normal activity
☐ 80 Normal activity with effort

Unable to work; able to live at home, care for most personal needs; a varying amount of assistance is needed.
☐ 70 Cares for self; unable to carry on normal activity or to do active work
☐ 60 Requires occasional assistance but is able to care for most needs
☐ 50 Requires considerable assistance and frequent medical care

Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.
☐ 40 Disabled; requires special care and assistance
☐ 30 Severely disabled; hospitalization indicated, although death not imminent
☐ 20 Very sick; hospitalization necessary
☐ 10 Moribund; fatal process progressing rapidly

Lansky Scale (age <16 yrs)
Select phrase which best describes the activity status:

Normal range.
☐ 100 Fully active
☐ 90 Minor restriction in physically strenuous play
☐ 80 Restricted in strenuous play, tires more easily, otherwise active

Mild to moderate restriction.
☐ 70 Both greater restrictions of, and less time spent in, active play
☐ 60 Ambulatory up to 50% of time, limited active play with assistance/supervision
☐ 50 Considerable assistance required for any active play; fully able to engage in quiet play

Moderate to severe restriction.
☐ 40 Able to initiate quiet activities
☐ 30 Needs considerable assistance for quiet activity
☐ 20 Limited to very passive activity initiated by others (i.e., TV)
☐ 10 Completely disabled, not even passive play

TEAM [ ][ ][ ]   IUBMID [.][ ][ ][ ][ ][ ]

6. Patient currently attends school:

  1 ☐ Yes ——┌─ **7.**   1 ☐ Part-time   2 ☐ Full-time   8 ☐ Unknown whether part-time or full-time

  0 ☐ No

                   8. Date returned to school: [ ][ ] [ ][ ]   or   ☐ Reported previously

                                            Month   Year

9. Patient was employed outside the home prior to current illness:

  1 ☐ Yes

  0 ☐ No

10. Patient has been employed outside the home since transplant:

  1 ☐ Yes ——┌─ **11.** Date returned to work: [ ][ ] [ ][ ]   or   ☐ Reported previously

  0 ☐ No   Month   Year

        └──────┐

                  12. Patient able to work but is not employed:

                       1 ☐ Yes

                       0 ☐ No

13. Patient has resumed all household activities:

  1 ☐ Yes ——┌─ **14.** Approximate date   [ ][ ] [ ][ ]   or   ☐ Reported previously

  0 ☐ No   resumed all activities: Month   Year

TEAM [ ][ ][ ]   IUBMID [ ][ ][ ][ ][ ][ ]

15. Did patient receive a blood or marrow infusion since the date of last report?
(other than peripheral blood leukocytes or T-lymphocytes from original allogeneic donor)

1 ☐ Yes ———
0 ☐ No

16. Date of subsequent infusion: [ ][ ] [ ][ ] [ ][ ]
                                    Month   Day   Year

17. Reason for subsequent infusion:
   1 ☐ No engraftment
   2 ☐ Partial engraftment
   3 ☐ Late graft failure
   4 ☐ Persistent malignancy
   5 ☐ Relapse
   6 ☐ Planned second transplant, per protocol
   7 ☐ Other, specify: _____

18. Type of graft:
   1 ☐ Allogeneic, related ———
   2 ☐ Allogeneic, unrelated ———
   3 ☐ Autologous

19. Donor
   1 ☐ Same donor
   2 ☐ Different donor
   3 ☐ Not applicable, initial transplant was autologous

Source of cells:

	Yes	No	
20.	1 ☐	0 ☐	Cryopreserved
21.	1 ☐	0 ☐	Bone marrow
22.	1 ☐	0 ☐	Peripheral blood
23.	1 ☐	0 ☐	Umbilical cord blood
24.	1 ☐	0 ☐	Fetal tissue
25.	1 ☐	0 ☐	Other, specify: _____

Answers to all questions in this report should reflect clinical status immediately prior to start of conditioning for subsequent infusion. **A separate report covering the subsequent transplant must be submitted.**

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

26. *Allografts only:* Has patient received an infusion of peripheral blood leukocytes or T-lymphocytes from the original donor since date of last report?

1 ☐ Yes ——

0 ☐ No

27. Date first infusion given: ☐☐ ☐☐ ☐☐

                                        Month   Day   Year

28. Patient weight within 2 weeks of first infusion: ☐☐☐.☐ kg

29. Total number of infusions: ☐☐

30. Total dose of <u>mononuclear</u> cells infused: ☐☐☐.☐ $\times 10^{10}$

31. Were cells manipulated prior to infusion?

      1 ☐ Yes ——

      0 ☐ No

32. Indicate method:

        <u>Yes</u> <u>No</u>

        1 ☐   0 ☐   T-cell depletion

        1 ☐   0 ☐   CD34 selection

        1 ☐   0 ☐   Other, specify: _____

33. Indication for the infusion(s) of donor cells:

      1 ☐ Prophylaxis against B-cell lymphoproliferative disorder or viral infection

      2 ☐ Prophylaxis against relapse

      3 ☐ Treatment of relapse

      4 ☐ Treatment of B-cell lymphoproliferative disorder

      5 ☐ Treatment of viral infection, specify: _____

      6 ☐ Graft failure

      7 ☐ Other, specify: _____

If answers 3 – 7 were selected, then answers to all questions in this report should reflect clinical status immediately prior to infusion. **This is considered a transplant and a separate report covering this infusion and post-infusion events must be submitted.**

Hematopoietic Reconstitution

34. Has patient received hematopoietic growth factors or cytokines since last report?　　　1 ☐ Yes　　0 ☐ No

Coding for Indication of Therapy (below)
1. Intervention for delay/decline in Absolute Neutrophil Count (ANC)
2. Intervention for delay/decline in platelets
3. Intervention for delay/decline in both ANC and platelets
4. Intervention for delay/decline in red blood cell counts
5. Anti-leukemic or tumor agent to _prevent_ relapse
6. Anti-leukemic or tumor agent to _treat_ relapse
7. Other indication

Specify agents given:

		Yes No		Date Started Month Day Year		Date Stopped Month Day Year		Indication
G-CSF	**35.**	1☐ 0☐	**36.**	☐☐ ☐☐ ☐☐	**37.**	☐☐ ☐☐ ☐☐	**38.**	☐
GM-CSF	**39.**	1☐ 0☐	**40.**	☐☐ ☐☐ ☐☐	**41.**	☐☐ ☐☐ ☐☐	**42.**	☐
Erythropoietin	**43.**	1☐ 0☐	**44.**	☐☐ ☐☐ ☐☐	**45.**	☐☐ ☐☐ ☐☐	**46.**	☐
Thrombopoietin	**47.**	1☐ 0☐	**48.**	☐☐ ☐☐ ☐☐	**49.**	☐☐ ☐☐ ☐☐	**50.**	☐
Interleukin-2	**51.**	1☐ 0☐	**52.**	☐☐ ☐☐ ☐☐	**53.**	☐☐ ☐☐ ☐☐	**54.**	☐
Interleukin-3	**55.**	1☐ 0☐	**56.**	☐☐ ☐☐ ☐☐	**57.**	☐☐ ☐☐ ☐☐	**58.**	☐
Interleukin-6	**59.**	1☐ 0☐	**60.**	☐☐ ☐☐ ☐☐	**61.**	☐☐ ☐☐ ☐☐	**62.**	☐
PIXY-321	**63.**	1☐ 0☐	**64.**	☐☐ ☐☐ ☐☐	**65.**	☐☐ ☐☐ ☐☐	**66.**	☐
Stem Cell Factor (SCF)	**67.**	1☐ 0☐	**68.**	☐☐ ☐☐ ☐☐	**69.**	☐☐ ☐☐ ☐☐	**70.**	☐
Interferon-alpha	**71.**	1☐ 0☐	**72.**	☐☐ ☐☐ ☐☐	**73.**	☐☐ ☐☐ ☐☐	**74.**	☐
Interferon-gamma	**75.**	1☐ 0☐	**76.**	☐☐ ☐☐ ☐☐	**77.**	☐☐ ☐☐ ☐☐	**78.**	☐
Blinded growth factor trial, specify agent(s) being studied:	**79.**	1☐ 0☐	**80.**	☐☐ ☐☐ ☐☐	**81.**	☐☐ ☐☐ ☐☐	**82.**	☐
Other, specify:	**83.**	1☐ 0☐	**84.**	☐☐ ☐☐ ☐☐	**85.**	☐☐ ☐☐ ☐☐	**86.**	☐

87. Did patient receive other courses of growth factors or cytokines since last report?

1 ☐ Yes ── _Photocopy Q.35-86 and answer for each additional course given._
0 ☐ No
8 ☐ Unknown

NOTE: A _new course_ includes starting a new agent, restarting a previously administered agent for a new indication or restarting a previously administered agent for the same indication but ≥ 30 days after discontinuing the agent.

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐☐

Granulopoiesis

88. Did patient achieve an <u>initial</u> hematopoietic recovery (ANC $\geq$ 500/mm³ for 3 consecutive days) since last report?

1 ☐ Yes ————————

> **89.** Date ANC $\geq$ 500/mm³: ☐☐ ☐☐ ☐☐   ☐ Date unknown
> (*First of 3 consecutive days*)   Month Day Year
>
> **90.** Was ANC $\geq$ 1000/mm³ achieved and sustained for 3 consecutive days?
>
> 1 ☐ Yes ———
> 0 ☐ No
>
> > **91.** Date achieved: ☐☐ ☐☐ ☐☐   ☐ Date unknown
> >   Month Day Year
> >   (*first of 3 consecutive days*)
>
> [Go to Q. 92]

2 ☐ No, patient's initital hematopoietic recovery was recorded on a previous report ——— [Go to Q. 92]

3 ☐ No, patient has never achieved an ANC $\geq$ 500/mm³ for three consecutive days and there is no evidence of recurrent disease ——— [Go to Q. 96]

4 ☐ No, patient has never achieved an ANC $\geq$ 500/mm³ for three consecutive days and there was documented persistent malignant disease posttransplant ——— [Go to Q. 96]

92. Following initial hematopoietic recovery (ANC $\geq$ 500/mm³ for three consecutive days) did the patient experience a subsequent decline in ANC to < 500/mm³ for greater than three days <u>since last report</u>?

1 ☐ Yes ———————
0 ☐ No

[Go to Q. 117]

> **93.** Date of decline in ANC to < 500/mm³ for greater than 3 days: ☐☐ ☐☐ ☐☐
> (*First of 3 days that ANC declined*)   Month Day Year
>
> ☐ Date unknown
>
> **94.** Did patient recover and maintain ANC $\geq$ 500/mm³ following the decline?
>
> 1 ☐ Yes ———
> 0 ☐ No
>
> > **95.** Date of ANC recovery: ☐☐ ☐☐ ☐☐   ☐ Date unknown
> >   Month Day Year
>
> [Go to Q. 96]

TEAM ☐☐☐☐ IUBMID ☐.☐☐☐☐☐☐

Suspected etiology of failure to achieve ANC > 500/mm³ or of a decline in ANC:

96. Persistent disease or relapse:
- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

97. Graft versus host disease:
- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

98. Immune-mediated rejection:
- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

99. Non-viral infection:
- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

100. Suspected viral infection:
- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

Virus suspected:

	Yes	No	
101.	1 ☐	0 ☐	Cytomegalovirus (CMV)
102.	1 ☐	0 ☐	Human Herpes Virus Type 6 (HHV6)
103.	1 ☐	0 ☐	Herpes Simplex Virus (HSV)
104.	1 ☐	0 ☐	Varicella
105.	1 ☐	0 ☐	Other, specify:

106. Documented viral infection:
- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

Virus involved:

	Yes	No	
107.	1 ☐	0 ☐	Cytomegalovirus (CMV)
108.	1 ☐	0 ☐	Human Herpes Virus Type 6 (HHV6)
109.	1 ☐	0 ☐	Herpes Simplex Virus (HSV)
110.	1 ☐	0 ☐	Varicella
111.	1 ☐	0 ☐	Other, specify:

112. Drugs:
- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

	Yes	No	
113.	1 ☐	0 ☐	Ganciclovir
114.	1 ☐	0 ☐	Bactrim, Septra, Trimethoprim-sulfamethoxazole
115.	1 ☐	0 ☐	Other, specify:

116. Etiology undetermined:
- 1 ☐ Yes
- 0 ☐ No

TEAM [ ][ ][ ][ ]   IUBMID [ ][ ][ ][ ][ ][ ]

Megakaryopoiesis

*The following questions relate to **initial** platelet recovery. All dates should reflect no transfusions in previous 7 days, and the first of 3 consecutive laboratory results.*

117. Did recipient achieve an **initial** platelet count of $\geq 20 \times 10^9$/L <u>since last report</u>?

    1 ❑ Yes ──────── (Go to Q. 118)

    2 ❑ No, recipient achieved a platelet count of $\geq 20 \times 10^9$/L but $< 50 \times 10^9$/L <u>prior</u> to last report ──── (Go to Q. 119)

    3 ❑ No, recipient achieved a platelet count of $\geq 50 \times 10^9$/L but $< 100 \times 10^9$/L <u>prior</u> to last report ──── (Go to Q. 121)

    4 ❑ No, recipient achieved a platelet count of $\geq 100 \times 10^9$/L <u>prior</u> to last report ──── (Go to Q. 125)

    0 ❑ No, recipient never achieved a platelet count of $\geq 20 \times 10^9$/L ──── (Go to Q. 123)

118. Date platelets $\geq 20 \times 10^9$/L: [ ][ ] [ ][ ] [ ][ ] ❑ Date unknown
                                Month Day Year

119. Was a platelet count of $\geq 50 \times 10^9$/L achieved?

    1 ❑ Yes ───────────── | 120. Date platelets $\geq 50 \times 10^9$/L: [ ][ ] [ ][ ] . [ ][ ] ❑ Date unknown
    0 ❑ No ──── (Go to Q. 123) | Month Day Year
    8 ❑ Unknown ──┘

121. Was a platelet count of $\geq 100 \times 10^9$/L achieved?

    1 ❑ Yes ───────────── | 122. Date platelets $\geq 100 \times 10^9$/L: [ ][ ] [ ][ ] [ ][ ] ❑ Date unknown
    0 ❑ No | Month Day Year
    8 ❑ Unknown

123. Was recipient ever platelet transfusion independent?

    1 ❑ Yes ───── | 124. Date of the last platelet transfusion:*
    0 ❑ No

                              [ ][ ] [ ][ ] [ ][ ] ❑ Date unknown
                              Month Day Year

Go to Q. 125 if platelet count of $\geq 20 \times 10^9$/L achieved; otherwise go to Q. 133

*If recipient was platelet transfusion independent for ≥ 14 days but subsequently experienced a decline in platelet count and required platelet transfusions, record date of last platelet transfusion <u>before decline in counts</u>. If recipient has not required platelet transfusions since initial platelet recovery record date of last platelet transfusion.

125. After initial recovery to platelet count $\geq 20 \times 10^9$/L did the platelet count decline to $< 20 \times 10^9$/L for 3 consecutive laboratory values or decline to $< 20 \times 10^9$/L for one laboratory value and the recipient received a platelet transfusion?

1 ☐ Yes

2 ☐ No

Go to Q. 159 if platelet count of $\geq 100 \times 10^9$/L achieved, otherwise go to Q. 133

126. Date of the first day that platelet count declined below 20×10^9/L:

☐☐ ☐☐ ☐☐   ☐ Date unknown

Month   Day   Year

127. Has platelet count recovered?

1 ☐ Yes

0 ☐ No

Go to Q. 133

The following date questions relate to **subsequent** platelet recovery following a decline of platelet count to below 20×10^9/L. All dates should reflect no transfusions in previous 7 days, and the first of 3 consecutive laboratory values.

128. Was a platelet count of $\geq 20 \times 10^9$/L achieved?

1 ☐ Yes

0 ☐ No

Go to Q. 131

129. Was a platelet count of $\geq 50 \times 10^9$/L achieved?

1 ☐ Yes

0 ☐ No

Go to Q. 131

130. Was a platelet count of $\geq 100 \times 10^9$/L achieved?

1 ☐ Yes

0 ☐ No

131. Was patient ever transfusion independent following recovery from decline?

1 ☐ Yes

0 ☐ No

132. Date of the last platelet transfusion (following recovery from decline):

☐☐ ☐☐ ☐☐   ☐ Date unknown

Month   Day   Year

Suspected etiology of failure to achieve a platelet count $\geq 100 \times 10^9$/L or decline in platelet count to $< 20 \times 10^9$/L:

133. Persistent disease or relapse:

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

134. Graft versus host disease:

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

135. Non-viral infection:

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

136. Immune-mediated:

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

Immune mediated etiology:

		Yes	No	
137.		1 ☐	0 ☐	Cellular
138.		1 ☐	0 ☐	Antibody
139.		1 ☐	0 ☐	Third party engraftment
140.		1 ☐	0 ☐	Unknown

141. Suspected viral infection:

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

Virus suspected:

		Yes	No	
142.		1 ☐	0 ☐	Cytomegalovirus (CMV)
143.		1 ☐	0 ☐	Human Herpes Virus Type 6 (HHV6)
144.		1 ☐	0 ☐	Herpes Simplex Virus (HSV)
145.		1 ☐	0 ☐	Varicella
146.		1 ☐	0 ☐	Other, specify:

_____

147. Documented viral infection:

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

Virus involved:

		Yes	No	
148.		1 ☐	0 ☐	Cytomegalovirus (CMV)
149.		1 ☐	0 ☐	Human Herpes Virus Type 6 (HHV6)
150.		1 ☐	0 ☐	Herpes Simplex Virus (HSV)
151		1 ☐	0 ☐	Varicella
152.		1 ☐	0 ☐	Other, specify:

_____

153. Drugs:

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

Therapy:

		Yes	No	
154.		1 ☐	0 ☐	Ganciclovir
155.		1 ☐	0 ☐	Bactrim, Septra, Trimethoprim-sulfamethoxazole
156.		1 ☐	0 ☐	Other, specify:

_____

157. Veno-occlusive disease (VOD):

- 1 ☐ Yes
- 0 ☐ No
- 8 ☐ Unknown

158. Etiology undetermined:

- 1 ☐ Yes
- 0 ☐ No

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

Erythropoiesis

159. Has patient received red blood cell (RBC) transfusions <u>since last report</u>?

1 ☐ Yes ───

0 ☐ No

> **160.** Date of last RBC transfusion:* ☐☐ ☐☐ ☐☐   ☐ Date unknown
> Month   Day   Year
>
> *If patient was RBC transfusion independent for ≥ 1 month but subsequently experienced a decline in RBC count and required RBC transfusions, record date of last RBC transfusion <u>before decline in counts</u>. If patient has not required RBC transfusions since initial date of recovery, record date of last RBC transfusion.

Current Hematologic Findings

161. Date of most recent CBC: ☐☐ ☐☐ ☐☐
Month   Day   Year

Actual CBC results:

162. WBC ☐☐☐.☐ x 10^9/L

163. Neutrophils ☐☐ %

164. Lymphocytes ☐☐ %

165. Hemoglobin ☐☐.☐ g/dL   ☐ Transfused

166. Hematocrit ☐☐ %   ☐ Transfused

167. Platelets ☐☐ x 10^9/L   ☐ Transfused

168. Were chimerism studies performed since last report?

1 ☐ Yes ──(Complete following page)

0 ☐ No ──(Go to Q. 169)

TEAM ☐☐☐ IUBMID ☐☐☐☐☐☐

Autotransplants only
Chimerism Studies

(Provide date(s), method(s) and other information for all chimerism studies performed since date of last report)

Date			Method (See Valid List Below)	Cell Type (See Valid List Below)	Number of Cells Examined (Total Cells)	Number of Donor Cells	Number of Host Cells	Number of Unknown Origin (third party) Cells	Percent Donor Cells		Percent Host Cells		Percent Unknown Origin (third party) Cells	
Month	Day	Year							Quant.	*Non-Quant.	Quant.	*Non-Quant.	Quant.	*Non-Quant.
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐
☐☐	☐☐	☐☐	☐	☐	☐☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐	☐	☐☐	☐	☐☐	☐

Valid Method Codes
(Insert number in box above to indicate method used)
1 – Standard Cytogenetics
2 – Fluorescent In situ Hybridization (FISH)
3 – Restriction Fragment-length polymorphisms (RFLP)
4 – Polymerase Chain Reaction (PCR)
5 – HLA Serotyping
6 – VNTR
7 – Other, specify: _____

Valid Cell Types
(Insert number in box above to indicate cell type used)
1 – Bone Marrow (BM)
2 – Peripheral Blood Mononuclear Cells (PBMC)
3 – T-Cells
4 – B-Cells
5 – Red Cells
6 – Monocytes
7 – Neutrophils
8 – Other, specify: _____

* If performed by non-quantitative method, indicate the presence of donor, host or third party cells by (+)

TEAM ☐☐☐☐ IUBMID ☐.☐☐☐☐☐☐

Graft-vs-Host Disease (GVHD)

169. Was specific therapy used since last report to prevent <u>or induce</u> GVHD, or promote engraftment?

1 ☐ Yes ——————

0 ☐ No ——————

8 ☐ Unknown ——————

| Allografts: |
| Go to Q. 186 |

| Autografts: |
| Go to Q. 326 |

For each agent listed below indicate whether or not it was used to prevent or induce GVHD since last report:

	Yes	No	
170.	1 ☐	0 ☐	Methotrexate
171.	1 ☐	0 ☐	Cyclosporine
172.	1 ☐	0 ☐	FK 506 (Tacrolimus)
173.	1 ☐	0 ☐	Corticosteroids
174.	1 ☐	0 ☐	ALS, ALG, ATS, ATG
175.	1 ☐	0 ☐	Azathioprine
176.	1 ☐	0 ☐	Cyclophosphamide
177.	1 ☐	0 ☐	In vivo anti T-lymphocyte monoclonal antibody: ——

	Yes	No	
178.	1 ☐	0 ☐	Anti IL-2
179.	1 ☐	0 ☐	Anti CD 25
180.	1 ☐	0 ☐	Campath
181.	1 ☐	0 ☐	OKT3
182.	1 ☐	0 ☐	Other, specify: _____

183. 1 ☐ 0 ☐ In vivo immunotoxin, specify:

_____

184. 1 ☐ 0 ☐ Blinded randomized trial; specify agent being studied: _____

185. 1 ☐ 0 ☐ Other, specify: _____

186. Was acute GVHD present at time of last report?

1 ☐ Yes —— (Go to Q. 195)

0 ☐ No

187. Did acute GVHD develop since date of last report?

1 ☐ Yes ——————

0 ☐ No ——————

8 ☐ Unknown ——————

(Go to Q. 238)

188. Date of onset: ☐☐ ☐☐ ☐☐
   Month   Day   Year

What was diagnosis based on?

189. Histologic evidence:

1 ☐ Yes ——————

0 ☐ No

Sites:

	Yes	No	
190.	1 ☐	0 ☐	Skin
191.	1 ☐	0 ☐	Gut
192.	1 ☐	0 ☐	Liver
193.	1 ☐	0 ☐	Other, specify: _____

194. Clinical evidence:

1 ☐ Yes

0 ☐ No

TEAM ☐☐☐☐ IUBMID ☐·☐☐☐☐☐☐

195. Maximum overall grade since last report: 1 ☐ I 2 ☐ II 3 ☐ III 4 ☐ IV

List the maximum severity of organ involvement attributed to acute GVHD:

	<u>Stage 0</u>	<u>Stage 1</u>	<u>Stage 2</u>	<u>Stage 3</u>	<u>Stage 4</u>
196. Skin:	1 ☐ No rash	2 ☐ Maculopapular rash, <25% of body surface	3 ☐ Maculopapular rash, 25–50% of body surface	4 ☐ Generalized erythroderma	5 ☐ Generalized erythroderma with bullae formation and desquamation

197. Intestinal tract (use ml/day for adult patients and ml/m^2/day for pediatric patients):

0 ☐ No diarrhea
1 ☐ Diarrhea ≤500 ml/day or <280 ml/m^2/day

2 ☐ Diarrhea >500 but ≤1000 ml/day or 280–555 ml/m^2/day

3 ☐ Diarrhea >1000 but ≤1500 ml/day or 556–833 ml/m^2/day

4 ☐ Diarrhea >1500 ml/day or >833 ml/m^2/day

5 ☐ Severe abdominal pain, with or without ileus

198. Liver:

1 ☐ Bilirubin <2.0 mg/dL
2 ☐ Bilirubin 2.0–3.0 mg/dL
3 ☐ Bilirubin 3.1–6.0 mg/dL
4 ☐ Bilirubin 6.1–15.0 mg/dL
5 ☐ Bilirubin >15.0 mg/dL

199. Other organ involvement?

1 ☐ Yes ——
0 ☐ No

	Yes	No	
200.	1 ☐	0 ☐	Upper GI tract
201.	1 ☐	0 ☐	Lung
202.	1 ☐	0 ☐	Other, specify: _____

TEAM ☐☐☐☐ IUBMID ☐·☐☐☐☐☐

203. Was specific therapy used to **treat** acute GVHD since last report? 1 ☐ Yes 0 ☐ No

For each agent listed below indicate whether or not it was used to **treat** acute GVHD

	No, drug not given	Drug continued at prophylactic dose	Yes, drug started	Yes, dose increased	Still taking? Yes	No
204. Methotrexate	0 ☐	1 ☐	2 ☐	3 ☐	**205.** 1 ☐	0 ☐
206. Cyclosporine	0 ☐	1 ☐	2 ☐	3 ☐	**207.** 1 ☐	0 ☐
208. FK 506 (Tacrolimus)	0 ☐	1 ☐	2 ☐	3 ☐	**209.** 1 ☐	0 ☐
210. Systemic Corticosteroids	0 ☐	1 ☐	2 ☐	3 ☐	**211.** 1 ☐	0 ☐
212. Topical Corticosteroids	0 ☐	1 ☐	2 ☐	3 ☐	**213.** 1 ☐	0 ☐
214. ALS, ALG, ATS, ATG	0 ☐	1 ☐	2 ☐	3 ☐	**215.** 1 ☐	0 ☐
216. Azathioprine	0 ☐	1 ☐	2 ☐	3 ☐	**217.** 1 ☐	0 ☐
218. Cyclo-phosphamide	0 ☐	1 ☐	2 ☐	3 ☐	**219.** 1 ☐	0 ☐
220. Thalidomide	0 ☐	1 ☐	2 ☐	3 ☐	**221.** 1 ☐	0 ☐

In vivo anti–T–lymphocyte monoclonal antibody:

	No, drug not given	Drug continued at prophylactic dose	Yes, drug started	Yes, dose increased	Still taking? Yes	No
222. Anti IL-2	0 ☐	1 ☐	2 ☐	3 ☐	**223.** 1 ☐	0 ☐
224. Anti CD 25	0 ☐	1 ☐	2 ☐	3 ☐	**225.** 1 ☐	0 ☐
226. Campath	0 ☐	1 ☐	2 ☐	3 ☐	**227.** 1 ☐	0 ☐
228. OKT3	0 ☐	1 ☐	2 ☐	3 ☐	**229.** 1 ☐	0 ☐
230. Other, antibody specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**231.** 1 ☐	0 ☐
232. In vivo immunotoxin, specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**233.** 1 ☐	0 ☐
234. Blinded randomized trial; specify agent(s) being studied: _____	0 ☐	1 ☐	2 ☐	3 ☐	**235.** 1 ☐	0 ☐
236. Other, specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**237.** 1 ☐	0 ☐

TEAM [ ][ ][ ][ ]   IUBMID [ ][.][ ][ ][ ][ ]

238. Was chronic GVHD present at time of last report?

1 ☐ Yes
0 ☐ No

> **239.** Chronic GVHD is still present or was present at time of death:
>
> 1 ☐ Yes ── [Go to Q. 256]
> 0 ☐ No

240. Did clinical chronic GVHD develop since date of last report?

1 ☐ Yes
0 ☐ No
8 ☐ Unknown

[Go to Q. 326]

241. Date of onset: [ ][ ] [ ][ ] [ ][ ]
Month   Day   Year

242. Progressed from acute GVHD?

1 ☐ Yes
0 ☐ No

243. Karnofsky/Lansky score (see page 1) at diagnosis of chronic GVHD: [ ][ ][ ]

244. Platelet count at diagnosis of chronic GVHD: [ ][ ][ ][ ] . [ ] x 10^9/L

245. Total serum bilirubin at diagnosis of chronic GVHD: [ ][ ] . [ ]

Unit of measurement for bilirubin:

1 ☐ mg/dL
2 ☐ μmol/L

What was diagnosis based on?

246. Histologic evidence:

1 ☐ Yes
0 ☐ No

255. Clinical evidence:

1 ☐ Yes
0 ☐ No

Sites:

	Yes	No	
247.	1 ☐	0 ☐	Skin
248.	1 ☐	0 ☐	Gut
249.	1 ☐	0 ☐	Liver
250.	1 ☐	0 ☐	Buccal mucosa/lip
251.	1 ☐	0 ☐	Conjunctiva
252.	1 ☐	0 ☐	Lung
253.	1 ☐	0 ☐	Muscle
254.	1 ☐	0 ☐	Other, specify: _____

Continued on next page

256. Maximum grade of chronic GVHD:

   1 ☐ Limited (*Localized skin involvement and/or hepatic dysfunction due to chronic GVHD*)

   2 ☐ Extensive *(Generalized skin involvement; or localized skin involvement and/or hepatic dysfunction due to chronic GVHD, plus :*
        -Liver histology showing chronic aggressive hepatitis, bridging necrosis or cirrhosis; or,
        -Involvement of eye: Schirmer's test with < 5 mm wetting; or,
        -Involvement of minor salivary glands or oral mucosa demonstrated on labial biopsy; or,
        -Involvement of any other target organ)*

257. Overall severity: 1 ☐ Mild   2 ☐ Moderate   3 ☐ Severe

Indicate organ involvement with chronic GVHD from list below:

		Yes	No	
Skin/Hair:	**258.**	1☐	0☐	Subclinical (biopsy findings only)
	259.	1☐	0☐	Rash
	260.	1☐	0☐	Scleroderma
	261.	1☐	0☐	Dyspigmentation
	262.	1☐	0☐	Contractures
	263.	1☐	0☐	Alopecia
	264.	1☐	0☐	Other skin/hair involvement, specify: _____
Eyes:	**265.**	1☐	0☐	Dry eyes
	266.	1☐	0☐	Corneal erosion/conjunctivitis
	267.	1☐	0☐	Other eye involvement, specify: _____
Mouth:	**268.**	1☐	0☐	Lichenoid changes
	269.	1☐	0☐	Mucositis/ulcers
	270.	1☐	0☐	Other mouth involvement, specify: _____
Lung:	**271.**	1☐	0☐	Bronchiolitis obliterans
	272.	1☐	0☐	Other lung involvement, specify: _____
GI Tract:	**273.**	1☐	0☐	Esophageal involvement
	274.	1☐	0☐	Chronic nausea/vomiting
	275.	1☐	0☐	Chronic diarrhea
	276.	1☐	0☐	Malabsorption
	277.	1☐	0☐	Other GI tract involvement, specify: _____
Liver:	**278.**	1☐	0☐	Liver involvement, specify: _____
GU Tract:	**279.**	1☐	0☐	Vaginitis/stricture
	280.	1☐	0☐	Other GU involvement, specify: _____
Musculoskeletal:	**281.**	1☐	0☐	Arthritis
	282.	1☐	0☐	Myositis
	283.	1☐	0☐	Myasthenia
	284.	1☐	0☐	Other musculoskeletal involvement, specify: _____
Hematologic:	**285.**	1☐	0☐	Thrombocytopenia
	286.	1☐	0☐	Eosinophilia
	287.	1☐	0☐	Autoantibodies
	288.	1☐	0☐	Other hematologic involvement, specify: _____
Other:	**289.**	1☐	0☐	Specify: _____

TEAM [ ][ ][ ]   IUBMID [ ][ ][ ][ ][ ][ ]

290. Was specific therapy used to **treat** chronic GVHD since last report?   1 ☐ Yes   0 ☐ No —[Go to Q. 325]

For each agent listed below indicate whether or not it was used to **treat** chronic GVHD

	No, drug not given	Drug continued at prophylactic dose	Yes, drug started	Yes, dose increased	Still taking? Yes	No
291. ALS, ALG, ATS, ATG	0 ☐	1 ☐	2 ☐	3 ☐	**292.** 1 ☐	0 ☐
293. Azathioprine	0 ☐	1 ☐	2 ☐	3 ☐	**294.** 1 ☐	0 ☐
295. Cyclosporine	0 ☐	1 ☐	2 ☐	3 ☐	**296.** 1 ☐	0 ☐
297. FK 506 (Tacrolimus)	0 ☐	1 ☐	2 ☐	3 ☐	**298.** 1 ☐	0 ☐
299. Systemic Corticosteroids	0 ☐	1 ☐	2 ☐	3 ☐	**300.** 1 ☐	0 ☐
301. Topical Corticosteroids	0 ☐	1 ☐	2 ☐	3 ☐	**302.** 1 ☐	0 ☐
303. Cyclo-phosphamide	0 ☐	1 ☐	2 ☐	3 ☐	**304.** 1 ☐	0 ☐
305. Thalidomide	0 ☐	1 ☐	2 ☐	3 ☐	**306.** 1 ☐	0 ☐

In vivo anti-T-lymphocyte monoclonal antibody

	No, drug not given	Drug continued at prophylactic dose	Yes, drug started	Yes, dose increased	Still taking? Yes	No
307. Anti IL-2	0 ☐	1 ☐	2 ☐	3 ☐	**308.** 1 ☐	0 ☐
309. Anti CD 25	0 ☐	1 ☐	2 ☐	3 ☐	**310.** 1 ☐	0 ☐
311. Campath	0 ☐	1 ☐	2 ☐	3 ☐	**312.** 1 ☐	0 ☐
313. OKT3	0 ☐	1 ☐	2 ☐	3 ☐	**314.** 1 ☐	0 ☐
315. Other, antibody specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**316.** 1 ☐	0 ☐
317. In vivo immunotoxin, specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**318.** 1 ☐	0 ☐
319. Blinded randomized trial; specify agent(s) being studied: _____	0 ☐	1 ☐	2 ☐	3 ☐	**320.** 1 ☐	0 ☐
321. Other, specify: _____	0 ☐	1 ☐	2 ☐	3 ☐	**322.** 1 ☐	0 ☐

TEAM [ ][ ][ ] IUBMID [.][ ][ ][ ][ ][ ]

323. Is patient still receiving treatment for chronic GVHD?

    1 ☐ Yes

    0 ☐ No ──── **324.** Date last treatment was administered: [ ][ ] [ ][ ] [ ][ ]
                                                  Month   Day   Year

325. Is chronic GVHD still present?

    1 ☐ Yes

    0 ☐ No

    8 ☐ No symptoms, but patient still receiving treatment

TEAM ☐☐☐ IUBMID · ☐☐☐☐☐☐

326. Did patient develop clinically significant infection <u>since date of last report</u>?   1 ☐ Yes   0 ☐ No

Select site and organism from lists shown on the next page and place number in the appropriate spaces. If more than one site or organism was involved, list one site of infection and organism on the first line; second site and/or organism on second line.

			Site	Organism	Date of Onset Month	Day	Year	Did infection resolve? Yes No

327. ☐ Bacterial

    <u>Typical</u> First **328.** ☐☐ **329.** _____ **330.** ☐☐ ☐☐ ☐☐ **331.** 1☐ 0☐

            Second **332.** ☐☐ **333.** _____ **334.** ☐☐ ☐☐ ☐☐ **335.** 1☐ 0☐

    336. Other bacterium, specify: _____

    <u>Atypical</u> First **337.** ☐☐ **338.** B☐☐☐ **339.** ☐☐ ☐☐ ☐☐ **340.** 1☐ 0☐

            Second **341.** ☐☐ **342.** B☐☐☐ **343.** ☐☐ ☐☐ ☐☐ **344.** 1☐ 0☐

    345. Other atypical bacterium, specify: _____

346. ☐ Fungal

    First **347.** ☐☐ **348.** F☐☐☐ **349.** ☐☐ ☐☐ ☐☐ **350.** 1☐ 0☐

    Second **351.** ☐☐ **352.** F☐☐☐ **353.** ☐☐ ☐☐ ☐☐ **354.** 1☐ 0☐

    355. Other fungus, specify: _____

356. ☐ Viral

    First **357.** ☐☐ **358.** V☐☐☐ **359.** ☐☐ ☐☐ ☐☐ **360.** 1☐ 0☐

    Second **361.** ☐☐ **362.** V☐☐☐ **363.** ☐☐ ☐☐ ☐☐ **364.** 1☐ 0☐

    365. Other virus, specify: _____

366. ☐ Parasitic

    First **367.** ☐☐ **368.** P☐☐☐ **369.** ☐☐ ☐☐ ☐☐ **370.** 1☐ 0☐

    Second **371.** ☐☐ **372.** P☐☐☐ **373.** ☐☐ ☐☐ ☐☐ **374.** 1☐ 0☐

    375. Other parasite, specify: _____

376. ☐ No organism identified

    First **377.** ☐☐ **378.** O 5 0 9 **379.** ☐☐ ☐☐ ☐☐ **380.** 1☐ 0☐

    Second **381.** ☐☐ **382.** O 5 0 9 **383.** ☐☐ ☐☐ ☐☐ **384.** 1☐ 0☐

Codes for Common Sites of Infection

01	Blood/buffy coat	40	*Genito-Urinary Tract unspecified*
02	Disseminated – generalized, isolated at 3 or more distinct sites	41	Kidneys, renal pelvis, ureters and bladder
03	*Central Nervous System unspecified*	42	Prostate
04	Brain	43	Testes
05	Spinal cord	44	Fallopian tubes, uterus, cervix
06	Meninges and CSF	45	Vagina
10	*Gastrointestinal Tract unspecified*	50	*Skin unspecified*
11	Lips	51	Genital area
12	Tongue, oral cavity and oro-pharynx	52	Cellulitis
13	Esophagus	53	Herpes Zoster
14	Stomach	54	Rash, pustules or abscesses not typical of any of the above
15	Gallbladder and biliary tree (not hepatitis), pancreas	60	Central venous catheter, not otherwise specified
16	Small intestine	61	Catheter insertion site
17	Large intestine	62	Catheter tip
18	Feces/stool	70	Eyes
19	Peritoneum	75	Ear
20	Liver	80	*Other unspecified*
30	*Respiratory unspecified*	81	Joints
31	Upper airway and nasopharynx	82	Bone marrow
32	Laryngitis/larynx	83	Bone cortex (osteomyelitis)
33	Lower respiratory tract (lung)	84	Muscle (excluding cardiac)
34	Pleural cavity, pleural fluid	85	Cardiac (endocardium, myocardium, pericardium)
35	Sinuses	86	Lymph nodes
		87	Spleen

Codes for Commonly Reported Organisms

1. Bacteria

(Indicate code for atypical bacteria;
list bacterium for non-atypical bacteria.)

100 Atypical bacteria, not otherwise specified
101 Coxiella
102 Legionella
103 Leptospira
104 Listeria
105 Mycoplasma
106 Nocardia
107 Rickettsia
110 Tuberculosis, NOS (AFB, acid fast bacillus, Koch bacillus)
111 Typical tuberculosis (TB, Tuberculosis)
112 Mycobacteria (avium, bovium, intracellulare)
113 Chlamydia
119 Atypical bacteria – other, specify

2. Fungal Infections

200 Candida, not otherwise specified
201 Candida albicans
202 Candida krusei
203 Candida parapsilosis
204 Candida tropicalis
205 Torulopsis glabrata (a subspecies of candida)
209 Candida, other
210 Aspergillus, not otherwise specified
211 Aspergillus flavus
212 Aspergillus fumigatus
213 Aspergillus niger
219 Aspergillus, other
220 Cryptococcus species
230 Fusarium species
240 Mucormycosis (zygomycetes, rhizopus)
250 Yeast, not otherwise specified
259 Other fungus, specify

3. Viral Infections

301 Herpes Simplex (HSV1, HSV2)
302 Herpes Zoster (Chicken pox, Varicella)
303 Cytomegalovirus (CMV)
304 Adenovirus
305 Enterovirus (Coxsackie, Echo, Polio)
306 Hepatitis A (HAV)
307 Hepatitis B (HBV, Australian antigen)
308 Hepatitis C (HCV)
309 HIV-1 (HTLV-III)
310 Influenza
311 Measles (Rubeola)
312 Mumps
313 Papovavirus
314 Respiratory syncytial virus (RSV)
315 Rubella (German Measles)
316 Parainfluenza
317 Human herpesvirus-6 (HHV-6)
318 Epstein-Barr virus (EBV)
319 Polyomavirus
320 Rotavirus
321 Rhinovirus
329 Other Viral, specify

4. Parasite Infections

401 Pneumocystis (PCP)
402 Toxoplasma
403 Giardia
404 Cryptosporidium
409 Other parasite (amebiasis, echinococcal cyst, trichomonas – either vaginal or gingivitis), specify

5. Other Infections

509 No organism identified

TEAM ☐☐☐☐   IUBMID. ☐☐☐☐☐☐

Pulmonary function

385. Has patient developed interstitial pneumonitis (IPn) since date of last report?

> *Interstitial pneumonitis is characterized by hypoxia and diffuse interstitial infiltrates on chest x-ray not caused by fluid overload.*

1 ☐ Yes ──────

0 ☐ No

386. How many episodes of IPn occurred since date of last report? ☐

> *Note: If more than one episode of IPn, photocopy this page and complete Q. 385 – 406 for subsequent episode(s).*

387. Date of onset of IPn: ☐☐ ☐☐ ☐☐
Month   Day   Year

388. Were diagnostic tests other than radiographic studies done?

1 ☐ Yes ───

0 ☐ No

> Diagnosis was evaluated by:
>
> | | Yes | No | |
> |---|---|---|---|
> | **389.** | 1 ☐ | 0 ☐ | Bronchoalveolar lavage |
> | **390.** | 1 ☐ | 0 ☐ | Transbronchial biopsy |
> | **391.** | 1 ☐ | 0 ☐ | Open lung biopsy |
> | **392.** | 1 ☐ | 0 ☐ | Autopsy |
> | **393.** | 1 ☐ | 0 ☐ | Other, specify: _____ |

394. Was an organism isolated?

1 ☐ Yes ───

0 ☐ No (idiopathic, or no organism isolated)

> Etiology:
>
> | | Yes | No | |
> |---|---|---|---|
> | **395.** | 1 ☐ | 0 ☐ | Pneumocystis carinii |
> | **396.** | 1 ☐ | 0 ☐ | Aspergillus |
> | **397.** | 1 ☐ | 0 ☐ | Candida |
> | **398.** | 1 ☐ | 0 ☐ | Toxoplasma |
> | **399.** | 1 ☐ | 0 ☐ | Respiratory syncytial virus |
> | **400.** | 1 ☐ | 0 ☐ | Cytomegalovirus |
> | **401.** | 1 ☐ | 0 ☐ | Herpes simplex |
> | **402.** | 1 ☐ | 0 ☐ | Adenovirus |
> | **403.** | 1 ☐ | 0 ☐ | Human herpes virus 6 |
> | **404.** | 1 ☐ | 0 ☐ | Other virus, specify: _____ |
> | **405.** | 1 ☐ | 0 ☐ | Other, specify: _____ |

406. Has interstitial pneumonitis resolved?

1 ☐ Yes

0 ☐ No

8 ☐ Unknown

TEAM ☐☐☐   IUBMID ☐☐☐☐☐☐

407. Did patient develop pulmonary abnormalities other than interstitial pneumonitis since date of last report?

1 ☐ Yes
0 ☐ No

408. Did patient develop Acute Respiratory Distress Syndrome (ARDS) since last report?

1 ☐ Yes
0 ☐ No

409. Date of onset of ARDS: ☐☐ ☐☐ ☐☐
                Month Day Year

410. Were diagnostic tests done?

1 ☐ Yes
0 ☐ No

Diagnosis was evaluated by:

	Yes	No	
411.	1 ☐	0 ☐	Bronchoalveolar lavage
412.	1 ☐	0 ☐	Transbronchial biopsy
413.	1 ☐	0 ☐	Open lung biopsy
414.	1 ☐	0 ☐	Autopsy
415.	1 ☐	0 ☐	Other, specify: _____

416. Did patient develop bronchiolitis obliterans since last report?

1 ☐ Yes
0 ☐ No

417. Date of onset: ☐☐ ☐☐ ☐☐
                Month Day Year

418. Were diagnostic tests done?

1 ☐ Yes
0 ☐ No

Diagnosis was evaluated by:

	Yes	No	
419.	1 ☐	0 ☐	Bronchoalveolar lavage
420.	1 ☐	0 ☐	Transbronchial biopsy
421.	1 ☐	0 ☐	Open lung biopsy
422.	1 ☐	0 ☐	Autopsy
423.	1 ☐	0 ☐	Other, specify: _____

424. Did patient develop pulmonary hemorrhage since last report?

1 ☐ Yes
0 ☐ No

425. Date of onset: ☐☐ ☐☐ ☐☐
                Month Day Year

426. Were diagnostic tests done?

1 ☐ Yes
0 ☐ No

Diagnosis was evaluated by:

	Yes	No	
427.	1 ☐	0 ☐	Bronchoalveolar lavage
428.	1 ☐	0 ☐	Transbronchial biopsy
429.	1 ☐	0 ☐	Open lung biopsy
430.	1 ☐	0 ☐	Autopsy
431.	1 ☐	0 ☐	Other, specify: _____

432. Did patient develop other non-infectious pulmonary abnormalities since last report?

1 ☐ Yes
0 ☐ No

433. Specify: _____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

Liver function

434. Did patient develop non-infectious liver toxicity since last report?

1 ☐ Yes ————

0 ☐ No

> **435.** What was the date of onset? ☐☐ ☐☐ ☐☐
>   Month   Day   Year
>
> Etiology:
>
>   Yes No
> **436.** 1 ☐ 0 ☐   Veno-occlusive disease
> **437.** 1 ☐ 0 ☐   Other, specify: _____
> **438.** 1 ☐ 0 ☐   Unknown
>
> **439.** Has liver toxicity resolved?
>
>   1 ☐ Yes
>   0 ☐ No
>   8 ☐ Unknown

440. Did patient develop any other non-infectious clinically significant organ impairment or disorder since last report?

1 ☐ Yes ————

0 ☐ No

>   Yes No
> **441.** 1 ☐ 0 ☐   Renal failure requiring dialysis
> **442.** 1 ☐ 0 ☐   TTP/HUS or similar syndrome
> **443.** 1 ☐ 0 ☐   Hemorrhage, specify site:
>
> >   Yes No
> > **444.** 1 ☐ 0 ☐   CNS
> > **445.** 1 ☐ 0 ☐   Upper GI tract
> > **446.** 1 ☐ 0 ☐   Lower GI tract
> > **447.** 1 ☐ 0 ☐   Other, specify: _____
>
> **448.** 1 ☐ 0 ☐   Hemorrhagic cystitis
> **449.** 1 ☐ 0 ☐   Seizures
> **450.** 1 ☐ 0 ☐   Cataracts
> **451.** 1 ☐ 0 ☐   Avascular necrosis
> **452.** 1 ☐ 0 ☐   Hypothyroidism
> **453.** 1 ☐ 0 ☐   Gonadal dysfunction
> **454.** 1 ☐ 0 ☐   Growth hormone deficiency/growth disturbance
> **455.** 1 ☐ 0 ☐   Other, specify: _____

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐☐

456. Did a <u>new</u> malignancy, lymphoproliferative or myeloproliferative disorder appear since last report? *(If more than one new malignancy developed, copy this page and complete for each new cancer)*

1 ☐ Yes ──

0 ☐ No

457. Date of diagnosis: ☐☐ ☐☐ ☐☐

Month　Day　Year

458. Origin of cells:

1 ☐ Host　　8 ☐ Unknown

2 ☐ Donor　 7 ☐ Not tested

Diagnosis (**send copy of pathology report/other documentation**):

<u>Yes</u> <u>No</u>

459. 1 ☐ 0 ☐　Clonal cytogenetic abnormality without leukemia or MDS

460. 1 ☐ 0 ☐　Acute myeloid leukemia

461. 1 ☐ 0 ☐　Other leukemia, specify: _____

462. 1 ☐ 0 ☐　Myelodysplasia

463. 1 ☐ 0 ☐　Lymphoma or lymphoproliferative disease

464. EBV positive?　1 ☐ Yes　　0 ☐ No　　8 ☐ Unknown

465. 1 ☐ 0 ☐　Hodgkin disease

466. 1 ☐ 0 ☐　Other cancer

467. Primary site: _____

468. Histologic type: _____

469. Behavior:

1 ☐ Benign

2 ☐ In situ

3 ☐ Malignant/invasive

8 ☐ Unknown

TEAM ☐☐☐☐ IUBMID .☐☐☐☐☐☐

Death Information

470. Date of death: ☐☐ ☐☐ ☐☐
                        Month   Day   Year

Cause(s) of death:

Enter appropriate cause of death below. If a code number for "Other, specify" is entered, write the cause in the space provided.	**Cause of Death Codes**
	10 Graft rejection or failure
471. Primary: ☐☐☐ Specify: _____	20 Infection (other than interstitial pneumonia)
	21 Bacterial
Contributing or secondary causes:	22 Fungal
	23 Viral
472. ☐☐☐ Specify: _____	24 Protozoal
	25 Infection, organism not identified
	29 Other infection, specify
473. ☐☐☐ Specify: _____	30 Interstitial pneumonia
	31 Viral, CMV
474. ☐☐☐ Specify: _____	32 Viral, other
	33 Pneumocystis
	34 Fungus
475. ☐☐☐ Specify: _____	39 Other IPn, specify
	40 Adult Respiratory Distress Syndrome
476. ☐☐☐ Specify: _____	50 Acute GVHD
	60 Chronic GVHD
	70 Recurrence or persistence of primary disease
	NOTE: Code "70" may only be used as a primary cause of death, not a contributing or secondary cause.
	80 Organ failure (not due to GVHD or infection)
	81 Liver
	82 VOD
	83 Cardiac (Cardiomyopathy)
	84 Pulmonary
	85 CNS
	86 Renal
	89 Other organ failure, specify
	90 Secondary malignancy
	100 Hemorrhage
	110 Accidental death
	900 Other, specify

477. Was cause of death confirmed by autopsy?

1 ☐ Yes ─── **Send copy of autopsy report when available**
0 ☐ No
8 ☐ Unknown
6 ☐ Pending ───┘

FOLLOW-UP INSTITUTIONAL INFORMATION

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

(Institutional Unique Blood or Marrow
Transplant Identification Number)

Registry: IBMTR   ABMTR   (circle one)

Date of transplant for which
this form is being completed: ☐☐ ☐☐ ☐☐
                                 Month Day Year

Date of report: ☐☐ ☐☐ ☐☐
                  Month Day Year

---

1. Signed: _____ / _____

Person completing this form / Please print name

2. Date last report completed: ☐☐ ☐☐ ☐☐
                                      Month Day Year

3. Name of doctor for correspondence: _____

Institution: _____

Telephone: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Extension: ☐☐☐☐☐

Fax: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

4. Make reimbursement check payable to: _____

5. Patient or authorized family member/guardian is aware of, and has consented to, the fact that this case is being entered into the Registry database:

_____(physician's initials).

TEAM ☐☐☐   IUBMID ☐☐☐☐☐☐

(Institutional Unique Blood or Marrow Transplant Identification Number)

Date of transplant for which this form is being completed: ☐☐ ☐☐ ☐☐
Month Day Year

Date of report: ☐☐ ☐☐ ☐☐
Month Day Year

Pretransplant Information

If this is a report of a second (or subsequent) transplant, check here ☐ and go to Q.168

1. Date of pathologic diagnosis of breast cancer: ☐☐ ☐☐

   [Append copy of pathology report if available.]   Month Year

   If transplant was done after occurence of a second primary breast cancer, report staging and treatment [Q.1-75] of each primary separately by copying pages 1-4.

2. Stage of breast cancer at diagnosis:

   0 ☐ In situ
   1 ☐ I   - $T_1N_0M_0$
   2 ☐ II - $T_{0,1}N_1M_0$ or $T_2N_{0,1}M_0$ or $T_3N_0M_0$
   3 ☐ IIIA - $T_{0-2}N_2M_0$ or $T_3N_{1-2}M_0$
   4 ☐ IIIB - $T_4N_{Any}M_0$, $T_{Any}N_3M_0$, Inflammatory
   5 ☐ IV - $T_{Any}N_{Any}M_1$
   8 ☐ Unknown

3. Breast cancer histology at diagnosis:

   1 ☐ Invasive/infiltrating ductal
   2 ☐ Invasive lobular
   3 ☐ Inflammatory
   4 ☐ Other, specify: _____
   8 ☐ Unknown

4. Location of breast cancer at diagnosis:

   1 ☐ Right breast
   2 ☐ Left breast
   3 ☐ Bilateral

5. Menopausal status at diagnosis:

   1 ☐ Premenopausal
   2 ☐ Postmenopausal ——— 6. Age at menopause: ☐☐ years
   7 ☐ Not applicable, male patient
   8 ☐ Unknown

7. Did patient have a history of prior cancer (other than breast cancer)?

   1 ☐ Yes ———
   0 ☐ No

   8. Cite prior disease:
      1 ☐ Hodgkin lymphoma
      2 ☐ Non-Hodgkin lymphoma
      7 ☐ Other, specify: _____

   9. Date of diagnosis of prior cancer: ☐☐ ☐☐
      Month Year

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

10. Were metastases (other than ipsilateral axillary lymph nodes) present at diagnosis?

1 ☐ Yes

0 ☐ No

	Yes	No	Unknown	
11.	1 ☐	0 ☐	8 ☐	Bone
12.	1 ☐	0 ☐	8 ☐	Bone marrow
13.	1 ☐	0 ☐	8 ☐	Lung
14.	1 ☐	0 ☐	8 ☐	Liver
15.	1 ☐	0 ☐	8 ☐	Skin
16.	1 ☐	0 ☐	8 ☐	Chest wall
17.	1 ☐	0 ☐	8 ☐	Other lymph nodes, specify site: _____
18.	1 ☐	0 ☐	8 ☐	Other, specify: _____

19. Did patient receive neoadjuvant treatment (includes chemotherapy, hormones and/or radiation) prior to definitive surgery?

1 ☐ Yes

0 ☐ No ── Go to Q. 38

Neoadjuvant Treatment

Size of primary tumor (largest diameter before neoadjuvant treatment)

20. Was tumor multicentric?

1 ☐ Yes

0 ☐ No

8 ☐ Unknown

Give size of largest tumor in Q.21 – 22

21. Clinical size: ☐☐ cm   -7 ☐ Not measurable   -8 ☐ Unknown

22. Radiographic size: ☐☐ cm   -7 ☐ Not measurable   -8 ☐ Unknown

23. Did patient receive neoadjuvant **chemotherapy**?

1 ☐ Yes

0 ☐ No

Specify chemotherapy:

	Yes	No	
24.	1 ☐	0 ☐	Adriamycin alone
25.	1 ☐	0 ☐	CAF
26.	1 ☐	0 ☐	CMF
27.	1 ☐	0 ☐	AFM
28.	1 ☐	0 ☐	Other, specify: _____

29. Number of cycles: ☐

30. Did patient receive neoadjuvant **hormone therapy**?

1 ☐ Yes

0 ☐ No

Specify hormones:

	Yes	No	
31.	1 ☐	0 ☐	Tamoxifen
32.	1 ☐	0 ☐	Other, specify: _____

33. Duration of pre-surgical treatment was: ☐☐.☐ mos.

Continued on next page

TEAM [ ][ ][ ]   IUBMID [ ][ ][ ][ ][ ][ ]

34. Did patient receive neoadjuvant **radiation therapy?**

   1 ☐ Yes ———
   0 ☐ No

> **35.** Specify radiation field: _____
>
> **36.** Total dose: [ ][ ][ ] cGy (rads)

37. Best clinical response (at time of surgery) to neoadjuvant treatment:

   1 ☐ Complete response
   2 ☐ Partial response
   3 ☐ Stable disease
   4 ☐ Progressive disease
   8 ☐ Not evaluable, specify why not evaluable: _____

38. Did patient have surgery as part of initial management (include surgery done after neoadjuvant treatment)?

   1 ☐ Yes ———
   0 ☐ No

> **39.** Type of surgery was:
>
>   1 ☐ Mastectomy
>   2 ☐ Lumpectomy
>   7 ☐ Other, specify: _____

Size of primary tumor at time of definitive surgery; or, if surgery was not done, prior to initial non-surgical treatment

40. Was tumor multicentric?

   1 ☐ Yes
   0 ☐ No

Give size of largest tumor in Q.41 – 43

41. Clinical size: [ ][ ] cm   -8 ☐ Unknown

42. Radiographic size: [ ][ ] cm   -8 ☐ Unknown

43. Pathologic size: [ ][ ] cm   -8 ☐ Unknown

44. How many axillary nodes were examined? [ ][ ]   -8 ☐ Unknown

45. How many axillary nodes were positive for breast cancer? [ ][ ]   -8 ☐ Unknown

46. Were estrogen receptor assays done?

   1 ☐ Yes ———
   0 ☐ No
   8 ☐ Unknown

> **47.** Results:
>   1 ☐ Positive   3 ☐ Borderline
>   2 ☐ Negative   8 ☐ Unknown
>
> **48.** Actual value if available (specify units): [ ][ ][ ][ ]
>
> > **49.** Units:
> >   1 ☐ fmol/mg
> >   7 ☐ Other, specify: _____

50. Were progesterone receptor assays done?

   1 ☐ Yes ———
   0 ☐ No
   8 ☐ Unknown

> **51.** Results:
>   1 ☐ Positive   3 ☐ Borderline
>   2 ☐ Negative   8 ☐ Unknown
>
> **52.** Actual value if available (specify units): [ ][ ][ ][ ]
>
> > **53.** Units:
> >   1 ☐ fmol/mg
> >   7 ☐ Other, specify: _____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

54. Did patient receive radiation, chemotherapy and/or hormone treatment (excluding neoadjuvant) after definitive surgery as part of initial management?

1 ☐ Yes ————

0 ☐ No

55. Did patient receive radiation treatment?

1 ☐ Yes ————

0 ☐ No

Radiation field:		
	Yes	**No**
56.	1 ☐	0 ☐ local/regional
57.	1 ☐	0 ☐ sites of distant metastatic disease
58.	1 ☐	0 ☐ Other, specify: _____

59. Total dose: ☐☐☐☐ cGy (rads)

60. Did patient receive hormones?

1 ☐ Yes ————

0 ☐ No

Specify hormones:		
	Yes	**No**
61.	1 ☐	0 ☐ Tamoxifen
62.	1 ☐	0 ☐ Other, specify: _____

63. Date started: ☐☐ ☐☐
　　　　　　　　Month　Year

64. Date ended: ☐☐ ☐☐
　　　　　　　　Month　Year

65. Did patient receive chemotherapy?

1 ☐ Yes ————

0 ☐ No

66. Reason for chemotherapy:
　　1 ☐ Adjuvant
　　2 ☐ For metastatic disease ——— (Go to Q.79)

Chemotherapy given:		
	Yes	**No**
67.	1 ☐	0 ☐ CMF
68.	1 ☐	0 ☐ CAF
69.	1 ☐	0 ☐ Adriamycin-containing regimen
70.	1 ☐	0 ☐ Taxol alone
71.	1 ☐	0 ☐ Taxol plus other drugs
72.	1 ☐	0 ☐ Other chemotherapy, specify:

_____

73. Number of cycles: ☐☐　-8 ☐ Unknown

74. Date started: ☐☐ ☐☐
　　　　　　　　Month　Year

75. Date ended: ☐☐ ☐☐
　　　　　　　　Month　Year

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

76. Did breast cancer recur?

1 ☐ Yes ───── **77. Date:** ☐☐ ☐☐
0 ☐ No   Month   Year

78. Site(s): _____

79. Did patient receive treatment for persistent, recurrent or metastatic disease? 1 ☐ Yes   0 ☐ No

Regimen	Date Started	Date Stopped	Number cycles (chemotherapy)	Total dose (radiation)	Non-bone Response (see below)	Bone Response (see below)	Date Relapse/ Progression
1st	**80.** ☐☐ ☐☐ Month Year	**81.** ☐☐ ☐☐ Month Year	**82.** ☐☐☐	**83.** ☐☐☐☐☐ cGy (rads)	**84.** ☐	**85.** ☐	**86.** ☐☐ ☐☐ Month Year

Treatment, specify all drugs given:

   Yes No
87. 1☐ 0☐ Adriamycin   91. 1☐ 0☐ Methotrexate   94. 1☐ 0☐ Thiotepa
88. 1☐ 0☐ Cytoxan   92. 1☐ 0☐ Mitoxantrone   95. 1☐ 0☐ Vinblastine
89. 1☐ 0☐ Cisplatin   93. 1☐ 0☐ Taxol   96. 1☐ 0☐ Other, specify:
90. 1☐ 0☐ 5-fluorouracil (5-FU)   _____

| 2nd | **97.** ☐☐ ☐☐ Month Year | **98.** ☐☐ ☐☐ Month Year | **99.** ☐☐ | **100.** ☐☐☐☐☐ cGy (rads) | **101.** ☐ | **102.** ☐ | **103.** ☐☐ ☐☐ Month Year |

Treatment, specify all drugs given:

   Yes No
104. 1☐ 0☐ Adriamycin   108. 1☐ 0☐ Methotrexate   111. 1☐ 0☐ Thiotepa
105. 1☐ 0☐ Cytoxan   109. 1☐ 0☐ Mitoxantrone   112. 1☐ 0☐ Vinblastine
106. 1☐ 0☐ Cisplatin   110. 1☐ 0☐ Taxol   113. 1☐ 0☐ Other, specify:
107. 1☐ 0☐ 5-fluorouracil (5-FU)   _____

| 3rd | **114.** ☐☐ ☐☐ Month Year | **115.** ☐☐ ☐☐ Month Year | **116.** ☐☐ | **117.** ☐☐☐☐☐ cGy (rads) | **118.** ☐ | **119.** ☐ | **120.** ☐☐ ☐☐ Month Year |

Treatment, specify all drugs given:

   Yes No
121. 1☐ 0☐ Adriamycin   125. 1☐ 0☐ Methotrexate   128. 1☐ 0☐ Thiotepa
122. 1☐ 0☐ Cytoxan   126. 1☐ 0☐ Mitoxantrone   129. 1☐ 0☐ Vinblastine
123. 1☐ 0☐ Cisplatin   127. 1☐ 0☐ Taxol   130. 1☐ 0☐ Other, specify:
124. 1☐ 0☐ 5-fluorouracil (5-FU)   _____

Non-bone response codes:
1 = CR
2 = PR
3 = stable disease
4 = progressive disease

Bone response codes:
1 = no prior bone disease
2 = symptomatic improvement, no progression
3 = symptomatic and radiographic (not bone scan only) improvement
4 = no response
5 = progressive disease
6 = not evaluable (radiographic data not available)

Continued on next page

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

Regimen	Date Started	Date Stopped	Number cycles (chemotherapy)	Total dose (radiation)	Non-bone Response (see below)	Bone Response (see below)	Date Relapse/ Progression
	131.	**132.**	**133.**	**134.**	**135.**	**136.**	**137.**
4th	☐☐ ☐☐ Month Year	☐☐ ☐☐ Month Year	☐☐	☐☐☐☐ cGy (rads)	☐	☐	☐☐ ☐☐ Month Year

Treatment, specify all drugs given:

Yes No
138. 1☐ 0☐ Adriamycin   142. 1☐ 0☐ Methotrexate   145. 1☐ 0☐ Thiotepa
139. 1☐ 0☐ Cytoxan   143. 1☐ 0☐ Mitoxantrone   146. 1☐ 0☐ Vinblastine
140. 1☐ 0☐ Cis-platin   144. 1☐ 0☐ Taxol   147. 1☐ 0☐ Other, specify:
141. 1☐ 0☐ 5-fluorouracil (5-FU)   _____

Regimen	Date Started	Date Stopped	Number cycles	Total dose	Non-bone Response	Bone Response	Date Relapse/ Progression
	148.	**149.**	**150.**	**151.**	**152.**	**153.**	**154.**
5th	☐☐ ☐☐ Month Year	☐☐ ☐☐ Month Year	☐☐	☐☐☐☐ cGy (rads)	☐	☐	☐☐ ☐☐ Month Year

Treatment, specify all drugs given:

Yes No
155. 1☐ 0☐ Adriamycin   159. 1☐ 0☐ Methotrexate   162. 1☐ 0☐ Thiotepa
156. 1☐ 0☐ Cytoxan   160. 1☐ 0☐ Mitoxantrone   163. 1☐ 0☐ Vinblastine
157. 1☐ 0☐ Cis-platin   161. 1☐ 0☐ Taxol   164. 1☐ 0☐ Other, specify:
158. 1☐ 0☐ 5-fluorouracil (5-FU)   _____

Non-bone response codes:
1 = CR
2 = PR
3 = stable disease
4 = progressive disease

Bone response codes:
1 = no prior bone disease
2 = symptomatic improvement, no progression
3 = symptomatic and radiographic (not bone scan only) improvement
4 = no response
5 = progressive disease
6 = not evaluable (radiographic data not available)

What was the total dose of anthracyclines prior to start of high-dose therapy (conditioning)?

165. Doxorubicin: ☐☐☐ mg/m²   -8 ☐ Unknown   -7 ☐ Not given
     (Adriamycin)

166. Mitoxantrone: ☐☐☐ mg/m²   -8 ☐ Unknown   -7 ☐ Not given

167. Other ☐☐☐ mg/m²   -8 ☐ Unknown   -7 ☐ Not given
     anthracycline,
     specify: _____

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

168. Was bone marrow biopsy done <u>prior to high-dose conditioning</u>?

1 ☐ Yes ─

0 ☐ No

> **169.** Date of most recent biopsy ☐☐ ☐☐ ☐☐
> Month   Day   Year
>
> **170.** Was breast cancer present?
>
> 1 ☐ Yes ─
>
> 0 ☐ No
>
> > How was it detected?
> >
> > | | Yes | No | Not tested | |
> > |---|---|---|---|---|
> > | **171.** | 1 ☐ | 0 ☐ | 7 ☐ | Routine histopathology |
> > | **172.** | 1 ☐ | 0 ☐ | 7 ☐ | PCR (polymerase chain reaction) |
> > | **173.** | 1 ☐ | 0 ☐ | 7 ☐ | Other molecular technique |
> > | **174.** | 1 ☐ | 0 ☐ | 7 ☐ | Immunohistochemistry |
> > | **175.** | 1 ☐ | 0 ☐ | 7 ☐ | Cell culture technique |
> > | **176.** | 1 ☐ | 0 ☐ | 7 ☐ | Other, specify: _____ |

177. Did patient <u>ever</u> have bone marrow involvement with breast cancer other than involvement indicated in Q.168?

1 ☐ Yes ─

0 ☐ No

> How was it detected?
>
> | | Yes | No | Not tested | |
> |---|---|---|---|---|
> | **178.** | 1 ☐ | 0 ☐ | 7 ☐ | Routine histopathology |
> | **179.** | 1 ☐ | 0 ☐ | 7 ☐ | PCR (polymerase chain reaction) |
> | **180.** | 1 ☐ | 0 ☐ | 7 ☐ | Other molecular technique |
> | **181.** | 1 ☐ | 0 ☐ | 7 ☐ | Immunohistochemistry |
> | **182.** | 1 ☐ | 0 ☐ | 7 ☐ | Cell culture technique |
> | **183.** | 1 ☐ | 0 ☐ | 7 ☐ | Other, specify: _____ |

184. What was status of disease <u>immediately prior to start of conditioning</u>?

1 ☐ Complete response - no evidence of disease

2 ☐ Complete response with exception of bone scan abnormalities of unknown significance

3 ☐ Partial response

4 ☐ Stable

5 ☐ Progressive disease

Indicate all sites of disease involvement:

	At any time between diagnosis and transplant				Immediately prior to start of conditioning		
		Yes	No	Unknown		Yes	No	Unknown
Breast	185.1.	1 ☐	0 ☐	8 ☐	185.2.	1 ☐	0 ☐	8 ☐
Chest wall	186.1.	1 ☐	0 ☐	8 ☐	186.2.	1 ☐	0 ☐	8 ☐
Bone - symptomatic	187.1.	1 ☐	0 ☐	8 ☐	187.2.	1 ☐	0 ☐	8 ☐
Bone - radiographic	188.1.	1 ☐	0 ☐	8 ☐	188.2.	1 ☐	0 ☐	8 ☐
Axillary lymph nodes	189.1.	1 ☐	0 ☐	8 ☐	189.2.	1 ☐	0 ☐	8 ☐
Other lymph nodes	190.1.	1 ☐	0 ☐	8 ☐	190.2.	1 ☐	0 ☐	8 ☐
Brain	191.1.	1 ☐	0 ☐	8 ☐	191.2.	1 ☐	0 ☐	8 ☐
Lung	192.1.	1 ☐	0 ☐	8 ☐	192.2.	1 ☐	0 ☐	8 ☐
Pleura	193.1.	1 ☐	0 ☐	8 ☐	193.2.	1 ☐	0 ☐	8 ☐
Liver	194.1.	1 ☐	0 ☐	8 ☐	194.2.	1 ☐	0 ☐	8 ☐
Skin	195.1.	1 ☐	0 ☐	8 ☐	195.2.	1 ☐	0 ☐	8 ☐
Other, specify:	196.1.	1 ☐	0 ☐	8 ☐	196.2.	1 ☐	0 ☐	8 ☐

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

197. What was sensitivity of breast cancer to chemotherapy prior to conditioning? *(Response to last chemotherapy given prior to transplant; chemotherapy must include ≥ 2 cycles treatment given ≤ 6 months prior to transplant)*

1 ☐ Sensitive: ≥ 50% reduction in bidimensional diameter of all disease sites with no new sites of disease

2 ☐ Resistant: < 50% reduction in diameter of all disease sites or development of new disease sites

3 ☐ Untreated

8 ☐ Unknown

Outcome

198. What was patient's best response to transplant <u>excluding</u> planned posttransplant treatment?

1 ☐ Complete response: complete disappearance of all known disease for ≥ 4 weeks

2 ☐ Complete response with persistent bone scan/x-ray abnormalities of unknown significance

3 ☐ Partial response: ≥ 50% reduction in greatest diameter of all sites of known disease and no new sites of disease for ≥ 4 weeks

4 ☐ No response: < 50% reduction in greatest diameter of all sites of known disease and no new sites of disease

5 ☐ Progressive disease: increase in size of sites of known disease or new sites of disease

6 ☐ Not evaluable, toxic death

7 ☐ Not evaluable, other reason, specify: _____

199. Was planned treatment (treatment before progressive disease) given <u>posttransplant</u>?

1 ☐ Yes ——

0 ☐ No

[Go to Q.207]

200. Was disease restaged prior to planned posttransplant treatment?

1 ☐ Yes

0 ☐ No

<u>Specify treatment given whether restaged or not:</u>

	Yes	No	
201.	1 ☐	0 ☐	Chemotherapy, specify: _____
202.	1 ☐	0 ☐	Hormone therapy, specify: _____
203.	1 ☐	0 ☐	Radiation therapy, specify: _____
204.	1 ☐	0 ☐	Immune therapy, specify: _____
205.	1 ☐	0 ☐	Other, specify: _____

206. What was patient's best response to transplant <u>including</u> planned posttransplant treatment?

1 ☐ Complete response: complete disappearance of all known disease for ≥ 4 weeks

2 ☐ Complete response with persistent bone scan/x-ray abnormalities of unknown significance

3 ☐ Partial response: ≥ 50% reduction in greatest diameter of all sites of known disease and no new sites of disease for ≥ 4 weeks

4 ☐ No response: < 50% reduction in greatest diameter of all sites of known disease and no new sites of disease

5 ☐ Progressive disease: increase in size of sites of known disease or new sites of disease

6 ☐ Not evaluable, toxic death

7 ☐ Not evaluable, other reason, specify: _____

TEAM ☐☐☐☐ IUBMID ☐☐☐☐☐☐

207. Status of breast cancer: (*at time of this report or at time of death*)

  1 ☐ Free of breast cancer; no recurrence posttransplant

  2 ☐ Free of breast cancer except for persistent scan abnormalities of unknown significance, no recurrence posttransplant

  3 ☐ Persistent breast cancer without progression (*never achieved complete response*)

  4 ☐ Progressive disease (*never achieved complete response*)

         Date of progression ☐☐ ☐☐ ☐☐   Site(s): _____
                      Month   Day   Year

  5 ☐ Recurrent disease (relapse after complete response)

         Date of recurrence ☐☐ ☐☐ ☐☐   Site(s): _____
                      Month   Day   Year

  6 ☐ Free of breast cancer after posttransplant recurrence

         Date of recurrence ☐☐ ☐☐ ☐☐   Site(s): _____
                      Month   Day   Year

  7 ☐ Not evaluable; explain: _____

First site(s) of progression/recurrence:

	Yes	No	
208.	1 ☐	0 ☐	Lymph node
209.	1 ☐	0 ☐	Bone marrow
210.	1 ☐	0 ☐	CNS
211.	1 ☐	0 ☐	Liver
212.	1 ☐	0 ☐	Lung
213.	1 ☐	0 ☐	Local
214.	1 ☐	0 ☐	Contralateral breast
215.	1 ☐	0 ☐	Other, specify: _____

216. Date status established: ☐☐ ☐☐ ☐☐
                            Month   Day   Year

FOLLOW-UP: INSERT VIII
Breast Cancer

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

(Institutional Unique Blood or Marrow Transplant Identification Number)

Date of transplant for which this form is being completed: ☐☐ ☐☐ ☐☐
Month Day Year

Date of report: ☐☐ ☐☐ ☐☐
Month Day Year

Follow-up Information

* *Report data for date of last contact as reported in Q.3 of Follow-up Core Form or immediately prior to death.*

1. Was <u>planned</u> post transplant treatment (treatment before progressive disease) given since date of last report?

   1 ☐ Yes ———
   0 ☐ No
   |
   ⌐Go to Q.9⌐

   2. Was disease restaged prior to planned posttransplant treatment?

      1 ☐ Yes
      0 ☐ No

      <u>Specify treatment given whether restaged or not:</u>
          Yes No
      3. 1 ☐ 0 ☐ Chemotherapy, specify: _____
      4. 1 ☐ 0 ☐ Hormone therapy, specify: _____
      5. 1 ☐ 0 ☐ Radiation therapy, specify: _____
      6. 1 ☐ 0 ☐ Immune therapy, specify: _____
      7. 1 ☐ 0 ☐ Other, specify: _____

8. Specify best response to transplant <u>including</u> planned posttransplant treatment:

   1 ☐ Complete response (*complete disappearance of all known disease for ≥ 4 weeks*)
   2 ☐ Complete response with persistent bone scan or x-ray abnormalities of unknown significance
   3 ☐ Partial response (*≥ 50% reduction in greatest diameter of all sites of known disease and no new sites of disease for ≥ 4 weeks*)
   4 ☐ No response: < 50% reduction in greatest diameter of all sites of known disease and no new sites of disease
   5 ☐ Progressive disease: increase in size of sites of known disease or new sites of disease
       Specify site(s) of persistent/new disease: _____
   6 ☐ Not evaluable, toxic death
   7 ☐ Not evaluable, other reason, specify: _____

TEAM ☐☐☐☐   IUBMID ☐☐☐☐☐☐

---

9. Most recent status of breast cancer: (*for patients who died, report status at time of death*)

　1 ☐ Free of breast cancer; no recurrence posttransplant

　2 ☐ Free of breast cancer except for persistent scan abnormalities of unknown significance, no recurrence posttransplant

　3 ☐ Persistent breast cancer without progression (*never achieved CR or PR*)

　4 ☐ Progressive disease (*never achieved CR or PR*)

> Date of progression ☐☐ ☐☐ ☐☐ Site(s): _____
> Month　Day　Year

　5 ☐ Recurrent disease (relapse after complete remission)

> Date of progression ☐☐ ☐☐ ☐☐ Site(s): _____
> Month　Day　Year

　6 ☐ Free of breast cancer after posttransplant recurrence

> Date of recurrence ☐☐ ☐☐ ☐☐ Site(s): _____
> Month　Day　Year

　7 ☐ Not evaluable; explain: _____

10. Date current status established ☐☐ ☐☐ ☐☐
　　Month　Day　Year

First site(s) of progression/recurrence:

	Yes	No	
11.	1 ☐	0 ☐	Lymph node
12.	1 ☐	0 ☐	Bone marrow
13.	1 ☐	0 ☐	CNS
14.	1 ☐	0 ☐	Liver
15.	1 ☐	0 ☐	Lung
15.2	1 ☐	0 ☐	Local (chest wall)
15.3	1 ☐	0 ☐	Contralateral breast
16.	1 ☐	0 ☐	Other, specify:_____

NEW MALIGNANCY SUPPLEMENT FORM

For all patients with a new malignancy, complete one supplement form per patient (**send copy of pathology report/other documentation)**

Patient name: _____
IUBMID number: _____
Registry I.D: _____
Disease: _____
Date of Transplant: _____
Team Number: _____
Institution: _____
_____
_____
_____

Circle One: ABMTR   or   IBMTR

Did a <u>new</u> malignancy, lymphoproliferative or myeloproliferative disorder appear? *(If more than one new malignancy developed, copy this page and complete for each new cancer)*

1 ☐ Yes
0 ☐ No

Date of diagnosis: ☐☐ ☐☐ ☐☐
              Month Day Year

Origin of cells:
1 ☐ Host   8 ☐ Unknown
2 ☐ Donor   7 ☐ Not tested

Diagnosis (*send copy of pathology report/other documentation*):

Yes	No	
1 ☐	0 ☐	Clonal cytogenetic abnormality without leukemia or MDS
1 ☐	0 ☐	Acute myeloid leukemia
1 ☐	0 ☐	Other leukemia, specify: _____
1 ☐	0 ☐	Myelodysplasia
1 ☐	0 ☐	Lymphoma or lymphoproliferative disease

EBV positive? 1 ☐ Yes   0 ☐ No   8 ☐ Unknown

1 ☐	0 ☐	Hodgkin disease
1 ☐	0 ☐	Other cancer

Primary site: _____

Histologic type: _____

Behavior:
1 ☐ Benign
2 ☐ In situ
3 ☐ Malignant/invasive
8 ☐ Unknown
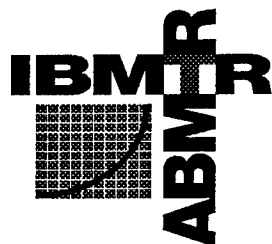
IBMTR and ABMTR Centers

			IBMTR	ABMTR
Alexander Fleming Institute	Buenos Aires	Argentina	✓	✓
Fundaleu / "Angelica Ocampo"	Buenos Aires	Argentina	✓	✓
Hospital de Pediatria, S.A.M.I.C.	Buenos Aires	Argentina	✓	
Hospital Privado de Oncologia	Buenos Aires	Argentina	✓	
Institutos Medicos Antartida ICTEM	Buenos Aires	Argentina	✓	
Navy Hospital Pedro Mallo	Buenos Aires	Argentina	✓	✓
Hospital Privado de Cordoba	Cordoba	Argentina	✓	✓
Hanson Centre for Cancer Research	Adelaide	Australia	✓	
Royal Brisbane Hospital	Brisbane	Australia	✓	
The Royal Children's Hospital	Brisbane	Australia	✓	
Royal Prince Alfred Hospital	Camperdown	Australia	✓	✓
St. Vincent's Hospital	Darlinghurst	Australia	✓	
Royal Children's Hospital	Parkville	Australia	✓	
Royal Melbourne Hospital	Parkville	Australia	✓	
Princess Margaret Hosp for Children	Perth	Australia	✓	
Royal Perth Hospital	Perth	Australia	✓	
Alfred Hospital	Prahran	Australia	✓	✓
Sydney Children's Hospital	Randwick	Australia	✓	
Royal North Shore Hospital	St. Leonards	Australia	✓	
Royal Alexandra Hospital for Children	Westmead	Australia	✓	
Westmead Hospital	Westmead	Australia	✓	
Ludwig Boltzmann Institut (LBI)	Vienna	Austria		✓
St. Anna Children's Hospital	Vienna	Austria	✓	
Univ. Klinik fur Innere Medizin I	Vienna	Austria	✓	
A.Z. Sint-Jan	Brugge	Belgium	✓	
Children University Hospital	Brussels	Belgium	✓	
Cliniques Universitaires Saint-Luc	Brussels	Belgium	✓	
Universiteit Antwerpen (UZA)	Edegem	Belgium	✓	
University Hospital Gasthuisberg	Leuven	Belgium	✓	
University of Liege	Liege	Belgium	✓	
Hemocentro/Univ. Estadual	Campinas	Brazil	✓	✓
Hospital de Clinicas	Curitiba	Brazil	✓	✓
Hospital Nossa Senhora das Gracas	Curitiba	Brazil		✓
Hospital das Clinicas	Ribeirao Preto	Brazil	✓	
Cent Nacional de Trans de Medula Ossea	Rio de Janeiro	Brazil	✓	
Univ Federal do Rio de Janeiro	Rio de Janerio	Brazil		✓
Hospital A.C. Camargo	Sao Paulo	Brazil	✓	
Instituto do Coracao INCOR	Sao Paolo	Brazil	✓	
Santa Casa Medical School - Sao Paulo	Sao Paulo	Brazil	✓	

			IBMTR	ABMTR
Alberta Children's Hospital	Calgary	Canada	✓	✓
University of Calgary	Calgary	Canada	✓	✓
Chedoke-McMaster Hospitals	Hamilton	Canada	✓	
London Health Sciences Center	London	Canada	✓	✓
Hopital Sainte-Justine	Montreal	Canada	✓	✓
Jewish General Hospital	Montreal	Canada		✓
Montreal Children's Hospital	Montreal	Canada	✓	✓
Royal Victoria Hospital	Montreal	Canada	✓	✓
Sacre Coeur Hospital	Montreal	Canada		✓
Ottawa General Hospital	Ottawa	Canada		✓
Hopital du Saint-Sacrement	Quebec City	Canada	✓	✓
Northeastern Ontario Reg Cancer Ctr	Sudbury	Canada		✓
Hospital for Sick Children	Toronto	Canada	✓	✓
Princess Margaret Hospital	Toronto	Canada	✓	
The Toronto Hosp & Ontario Cancer Inst	Toronto	Canada		✓
British Columbia's Children's Hospital	Vancouver	Canada	✓	✓
Vancouver Hosp and Health Sciences Ctr	Vancouver	Canada	✓	✓
Manitoba Cancer Treat. & Res Found	Winnipeg	Canada	✓	✓
Catholic University of Chile	Santiago	Chile	✓	
Bei Tai Ping Lu Hospital	Beijing	China	✓	
Beijing Medical University	Beijing	China	✓	
Centar za Transplataciju Kostane Srzi	Zagreb	Croatia	✓	
Institute de Hematologia e Immunologia	Havana	Cuba	✓	✓
Charles University Hospital	Pilsen	Czech Republic	✓	
Inst of Hematology & Blood Transfusion	Prague	Czech Republic	✓	
University Hospital Motol	Prague	Czech Republic	✓	
Rigshospitalet	Copenhagen	Denmark	✓	
NCI Cairo University	Cairo	Egypt	✓	
Helsinki University Central Hospital	Helsinki	Finland	✓	
Turku University Central Hospital	Turku	Finland	✓	
CHRU	Angers	France	✓	
Hopital Jean Minjoz	Besancon	France	✓	
Centre Hospitalier Regional de Lille	Lille	France	✓	
Hopital Edouard Herriot	Lyon	France	✓	
Hopital des Enfants Malades	Paris	France	✓	
Hopital Robert Debre	Paris	France	✓	
Hopital Saint Louis	Paris	France	✓	
Hotel Dieu de Paris	Paris	France	✓	
Center Henri Becquerel (C.R.L.C.C.)	Rouen	France	✓	
University Hospital Charite	Berlin	Germany	✓	
Universitatsklinikum Rudolf Virchow	Berlin	Germany	✓	
Heinrich-Heine-Universitat Dusseldorf	Dusseldorf	Germany	✓	
Albert-Ludwig University	Freiburg	Germany	✓	
Zentrum fur Knochenmark Transplant	Hamburg	Germany	✓	
Medizinische Hochschule Hannover	Hannover	Germany	✓	
Kinderklinik der Universitat Munchen	Munchen	Germany	✓	
Universitat Munchen	Munchen	Germany	✓	
Univ. Children's Hospital	Tubingen	Germany	✓	
Medizinische Universitatsklinik	Tubingen	Germany	✓	
Universitatsklinikum Ulm	Ulm/Donau	Germany	✓	
Deutsche Klinik fur Diagnostik GmbH	Weisbaden	Germany	✓	

			IBMTR	ABMTR
Evangelismos Hospital	Athens	Greece	✓	
Queen Mary Hospital	Hong Kong	Hong Kong	✓	
The Chinese University of Hong Kong	Shatin, New Territories	Hong Kong	✓	
National Institute of Hematology	Budapest	Hungary	✓	
Tata Memorial Hospital	Bombay	India	✓	
Shariati General Hospital	Tehran	Iran	✓	
St. James's Hospital	Dublin	Ireland	✓	
Hadassah Hebrew University Hospital	Jerusalem	Israel	✓	
Policlinico S. Orsola-Malphighi	Bologna	Italy	✓	
S. Orsola University Hospital	Bologna	Italy	✓	
Spedali Civili-Brescia	Brescia	Italy	✓	
Ospedale San Martino	Genoa	Italy	✓	
Ospedale de Pesaro	Pesaro	Italy	✓	
Cent Trapianti Midollo Osseo	Pescara	Italy	✓	
Ospedale San Camillo	Rome	Italy	✓	
University "La Sapienza"	Rome	Italy	✓	
University Tor Vergata	Rome	Italy	✓	
Ospedale Molinette	Torino	Italy	✓	
Ospedale Regina Margherita	Torino	Italy	✓	
Udine University Hospital	Udine	Italy	✓	
Chiba University School of Medicine	Chiba	Japan	✓	
Hyogo College of Medicine	Hyogo	Japan	✓	
Tokai University Hospital	Isehara	Japan	✓	
Kanazawa University School of Medicine	Kanazawa-shi	Japan	✓	
Niigata University Medical Hospital	Niigata	Japan	✓	
Osaka Med Ctr for Cancer & Cardio Disease	Osaka	Japan	✓	
Jichi Medical School	Tochigi-ken	Japan	✓	
National Cancer Center Hospital	Tokyo	Japan	✓	
Nihon University School of Medicine	Tokyo	Japan	✓	
School of Medicine, Keio University	Tokyo	Japan	✓	
Kanagawa Cancer Center	Yokohama	Japan	✓	
Jordan University Hospital	Amman	Jordan	✓	
Asan Medical Center	Seoul	Korea	✓	
Catholic University Medical College	Seoul	Korea	✓	
Samsung Medical Center	Seoul	Korea	✓	
Hospital Kuala Lumpur	Kuala Lumpur	Malaysia	✓	
University of Malaya Hospital	Kuala Lumpur	Malaysia	✓	
Inst. Nacional de Cancerologia	Mexico, D.F.	Mexico		✓
Hosp. Especialidades Centro Medico	Naucalpan	Mexico	✓	✓
Centro de Hematologia y Medicina Interna	Puebla	Mexico	✓	✓
Auckland Medical School	Auckland	New Zealand	✓	
University of Auckland Hospital	Auckland	New Zealand	✓	
Canterbury Health Laboratory	Christchurch	New Zealand	✓	
Wellington School of Medicine	Wellington	New Zealand	✓	
Medical University of Gdansk	Gdansk	Poland	✓	
Silesian Medical Academy	Katowice	Poland	✓	
I Klinika Chorob Dzieci	Poznan ul Szpitalna	Poland	✓	
K. Dluski Hospital	Wroclaw	Poland	✓	
Instituto Portugues de Oncologia	Lisbon	Portugal	✓	
Inst. Portugues Oncologia	Porto	Portugal	✓	✓
Clinical Hospital Number 6	Moscow	Russia	✓	

			IBMTR	ABMTR
National Research Center for Hematology	Moscow	Russia	✓	
Research Inst of Pediatric Hematology	Moscow	Russia	✓	
Petrov Research Institute of Oncology	St. Petersburg	Russia	✓	✓
Russian Inst of Hem and Blood Transfusion	St. Petersburg	Russia	✓	
King Faisal Specialist Hosp & Research Ctr	Riyadh	Saudi Arabia	✓	
Riyadh Armed Forces Hospital	Riyadh	Saudi Arabia	✓	
University Hospital	Bratislava	Slovak Republic	✓	
Cape Town Haematology Clinic & BMT Ctr	Cape Town	South Africa	✓	✓
Univ of Cape Town Medical School	Cape Town	South Africa	✓	
Univ of Witwatersrand Medical School	Johannesburg	South Africa	✓	
Hospital de la Santa Creui Sant Pau	Barcelona	Spain	✓	
Hospital General Vall d'Hebron	Barcelona	Spain	✓	✓
Hospital Infantil Vall d'Hebron	Barcelona	Spain	✓	
Institute Catala D'Oncologia	Barcelona	Spain	✓	
Postgraduate School of Haematology	Barcelona	Spain	✓	
Hospital NTRA Sra Del Pino	Islas Canarias	Spain	✓	
Hospital de la Princesa	Madrid	Spain	✓	
Hospital Infantil La Paz	Madrid	Spain	✓	
Hospital Nino Jesus	Madrid	Spain	✓	
Hospital Puerta de Hierro	Madrid	Spain	✓	
Son Dureta Hospital	Palma de Mallorca	Spain	✓	
Clinica Univ. de Navarra	Pamplona	Spain		✓
Hospital Marques de Valdecilla	Santander	Spain	✓	
Hospital La Fe	Valencia	Spain	✓	
University of Goteborg	Goteborg	Sweden	✓	
Huddinge Hospital	Huddinge	Sweden	✓	
University Hospital of Lund	Lund	Sweden	✓	
Kantonsspital	Basel	Switzerland	✓	
Kantonsspital Zurich	Zurich	Switzerland	✓	
Kinderspital Zurich	Zurich	Switzerland	✓	
Veteran's General Hospital-Taipei	Taipai	Taiwan	✓	
National Taiwan University Hospital	Taipei	Taiwan	✓	
Tri-Service General Hospital, N.D.M.C.	Taipei	Taiwan	✓	
Leiden University Hospital	Leiden	The Netherlands	✓	
University Hospital Maastricht	Maastricht	The Netherlands	✓	
University of Nijmegen	Nijmegen	The Netherlands	✓	
Dr. Daniel den Hoed Klinik	Rotterdam	The Netherlands	✓	
University Hospital Utrecht	Utrecht	The Netherlands	✓	
Ankara University Medical School	Ankara	Turkey	✓	
Gulhane Military Medical Academy	Ankara	Turkey	✓	✓
Birmingham Heartlands Hospital	Birmingham	UK	✓	
The Queen Elizabeth Hospital	Birmingham	UK	✓	
The Royal Infirmary of Edinburgh	Edinburgh, Scotland	UK	✓	
Glasgow Royal Infirmary	Glasgow, Scotland	UK	✓	
HCI International Medical Centre	Glasgow, Scotland	UK	✓	
Royal Hospital for Sick Children	Glasgow, Scotland	UK	✓	
St. James's University Hospital	Leeds	UK	✓	
Hospital for Sick Children	London	UK	✓	
The London Clinic	London	UK	✓	
Royal Free Hospital	London	UK	✓	
The Royal London Hospital	London	UK	✓	

			IBMTR	ABMTR
Royal Postgraduate Medical School	London	UK	✓	
St. George's Hospital Medical School	London	UK	✓	
The Royal Victoria Infirmary	Newcastle Upon Tyne	UK	✓	
Royal Marsden Hospital	Sutton	UK	✓	
British Hospital & Faculty of Medicine	Montevideo	Uruguay	✓	✓
Centro de Trasplante de Medula Ossea	Montevideo	Uruguay	✓	✓
Hosp Maciel Ministere of Public Health	Montevideo	Uruguay		✓
Albany Medical Center	Albany, NY	USA	✓	✓
Don & Sybil Harrington Cancer Center	Amarillo, TX	USA	✓	✓
University of Michigan Medical Center	Ann Arbor, MI	USA	✓	✓
Arlington Cancer Center	Arlington, TX	USA		✓
Atlanta Cancer Care	Atlanta, GA	USA		✓
Emory Clinic	Atlanta, GA	USA		✓
Southwest Regional Cancer Center	Austin, TX	USA		✓
Johns Hopkins Oncology Center	Baltimore, MD	USA	✓	✓
Univ of Maryland Cancer Ctr	Baltimore, MD	USA	✓	✓
Mary Bird Perkins Cancer Center	Baton Rouge, LA	USA		✓
Alta Bates Medical Center	Berkeley, CA	USA	✓	✓
National Heart, Lung & Blood Inst / NIH	Bethesda, MD	USA	✓	
University of Alabama at Birmingham	Birmingham, AL	USA	✓	✓
St. Luke's RMC/Mountain State Tumor Inst	Boise, ID	USA		✓
Brigham & Women's Hospital	Boston, MA	USA	✓	
Dana-Farber Cancer Institute	Boston, MA	USA		✓
Massachusetts General Hosp - MGH East	Boston, MA	USA	✓	
Montefiore Medical Center	Bronx, NY	USA		✓
Roswell Park Cancer Institute	Buffalo, NY	USA	✓	✓
Lahey Hitchcock Clinic	Burlington, MA	USA		✓
University of North Carolina, Chapel Hill	Chapel Hill, NC	USA	✓	✓
Medical University of South Carolina	Charleston, SC	USA	✓	✓
Children's Memorial Medical Center	Chicago, IL	USA	✓	✓
Michael Reese Hospital and Medical Center	Chicago, IL	USA	✓	✓
Mt. Sinai Hospital Medical Ctr	Chicago, IL	USA		✓
Northwestern Memorial Hospital	Chicago, IL	USA	✓	✓
Rush Presbyterian/St. Luke's Medical Ctr	Chicago, IL	USA	✓	✓
University of Chicago Medical Center	Chicago, IL	USA	✓	✓
Children's Hospital Medical Center	Cincinnati, OH	USA	✓	✓
The Jewish Hospital of Cincinnati	Cincinnati, OH	USA	✓	✓
Florida Community Cancer Center	Clearwater, FL	USA		✓
Cleveland Clinic Foundation	Cleveland, OH	USA	✓	✓
Rainbow Babies and Children's Hospital	Cleveland, OH	USA	✓	✓
University Hospitals of Cleveland	Cleveland, OH	USA	✓	✓
Rocky Mountain Cancer Center	Colorado Springs, CO	USA		✓
University of South Carolina	Columbia, SC	USA	✓	✓
Columbus Children's Hospital	Columbus, OH	USA	✓	✓
Ohio State University	Columbus, OH	USA	✓	✓
Baylor University Medical Center	Dallas, TX	USA	✓	✓
Children's Medical Center of Dallas	Dallas, TX	USA	✓	✓
Medical City Dallas Hospital	Dallas, TX	USA	✓	✓
Miami Valley Hospital	Dayton, OH	USA		✓
Halifax Medical Center	Daytona Beach, FL	USA		✓
Oakwood Hospital & Medical Center	Dearborn, MI	USA		✓

			IBMTR	ABMTR
The Children's Hospital	Denver, CO	USA	✓	
Rocky Mountain Cancer Center	Denver, CO	USA	✓	✓
Henry Ford Hospital	Detroit, MI	USA		✓
Wertz Clinical Center Center	Detroit, MI	USA	✓	✓
City of Hope National Medical Center	Duarte, CA	USA	✓	✓
Duke University Medical Center	Durham, NC	USA	✓	✓
St. Charles & John T. Mather Hospital	East Setauket, NY	USA		✓
Northwest Oncology & Hematology Assoc	Elk Grove Village, IL	USA		✓
Fairfax Hospital	Falls Church, VA	USA	✓	✓
University of Connecticut Health Center	Farmington, CT	USA		✓
Cook-Fort Worth Children's Medical Ctr	Fort Worth, TX	USA	✓	✓
KLABZUBA Cancer Center	Fort Worth, TX	USA	✓	✓
Bone Marrow/Stem Cell Institute of Florida	Ft. Lauderdale, FL	USA		✓
University of Florida	Gainesville, FL	USA	✓	
University of Florida, Shands Hospital	Gainesville, FL	USA	✓	✓
Cancer Center of the Carolinas	Greenville, SC	USA		✓
Hackensack Medical Center	Hackensack, NJ	USA		✓
James River Transplant Center	Hampton, VA	USA		✓
Hinsdale Hematology-Oncology Assoc	Hinsdale, IL	USA		✓
Queen's Medical Center	Honolulu, HI	USA		✓
St. Francis Medical Center	Honolulu, HI	USA	✓	✓
Baylor College of Medicine	Houston, TX	USA	✓	✓
MD Anderson Cancer Center	Houston, TX	USA	✓	✓
Texas Children's Hospital	Houston, TX	USA	✓	
Methodist Hospital of Indiana	Indianapolis, IN	USA	✓	✓
Oncology/Hematology Associates	Indianapolis, IN	USA		✓
St. Vincent Hospital & Health Care Center	Indianapolis, IN	USA		✓
Baptist Regional Cancer Center	Jacksonville, FL	USA		✓
Mayo Clinic Jacksonville/St. Luke's Hosp	Jacksonville, FL	USA	✓	✓
Saint Luke's Hospital of Kansas City	Kansas City, KS	USA	✓	✓
University of Kansas Medical Center	Kansas City, KS	USA	✓	✓
Children's Mercy Hospital	Kansas City, MO	USA	✓	✓
Scripps Clinic & Research Foundation	La Jolla, CA	USA		✓
University of California, San Diego	La Jolla, CA	USA	✓	✓
Dartmouth-Hitchcock Medical Center	Lebanon, NH	USA		✓
University of Kentucky Medical Center	Lexington, KY	USA	✓	✓
Univ of Arkansas for Medical Sciences	Little Rock, AR	USA	✓	✓
Children's Hospital of Los Angeles	Los Angeles, CA	USA	✓	
UCLA Center for Health Sciences	Los Angeles, CA	USA	✓	✓
USC/Kenneth Norris Jr. Cancer Ctr Hosp	Los Angeles, CA	USA		✓
University of Louisville	Louisville, KY	USA	✓	✓
University of Wisconsin Hospital & Clinics	Madison, WI	USA	✓	✓
North Shore University Hospital	Manhasset, NY	USA	✓	✓
Marshfield Clinic	Marshfield, WI	USA	✓	✓
Loyola University Medical Center	Maywood, IL	USA	✓	✓
Impact Center of Memphis	Memphis, TN	USA		✓
Methodist Hospital Central	Memphis, TN	USA		✓
St. Jude's Children's Research Hospital	Memphis, TN	USA	✓	✓
Baptist Hospital of Miami	Miami, FL	USA		✓
Miami Children's Hospital	Miami, FL	USA	✓	✓
Medical College of Wisconsin	Milwaukee, WI	USA	✓	✓

			IBMTR	ABMTR
St. Luke's Medical Center	Milwaukee, WI	USA		✓
Abbott Northwestern Hospital	Minneapolis, MN	USA		✓
University of Minnesota Hosp and Clinics	Minneapolis, MN	USA	✓	✓
Missoula Oncology & Infectious Disease	Missoula, MT	USA		✓
West Virginia University Hospitals	Morgantown, WV	USA	✓	✓
Children's Hospital, New Orleans	New Orleans, LA	USA	✓	✓
Louisiana State University Medical Center	New Orleans, LA	USA	✓	
Memorial Medical Center	New Orleans, LA	USA	✓	✓
Tulane University Medical Center	New Orleans, LA	USA	✓	✓
Columbia University	New York, NY	USA		✓
Memorial Sloan-Kettering Cancer Center	New York, NY	USA	✓	✓
Mount Sinai Medical Center	New York, NY	USA	✓	✓
Medical Center of Delaware	Newark, DE	USA	✓	✓
Hoag Cancer Center	Newport Beach, CA	USA		✓
Univ of Oklahoma Health Sciences Center	Oklahoma City, OK	USA	✓	✓
University of Nebraska Medical Center	Omaha, NE	USA	✓	✓
Children's Hospital of Orange County	Orange, CA	USA	✓	✓
St. Joseph Hospital	Orange, CA	USA	✓	✓
UCI Medical Ctr, Clinical Cancer Center	Orange, CA	USA	✓	✓
The Desert Hosp Comprehensive Cancer Ctr	Palm Springs, CA	USA		✓
Lutheran General Hospital	Park Ridge, IL	USA		✓
St. Joseph's Hospital & Medical Center	Paterson, NJ	USA	✓	
Hematology Assoicates	Peoria, IL	USA		✓
Children's Hospital of Philadelphia	Philadelphia, PA	USA	✓	✓
Hahnemann University Hospital	Philadelphia, PA	USA	✓	✓
Temple Univ Comprehensive Cancer Ctr	Philadelphia, PA	USA	✓	✓
Thomas Jefferson University Hospital	Philadelphia, PA	USA	✓	✓
University of Pennsylvania Hospital	Philadelphia, PA	USA		✓
Children's Hospital of Pittsburgh	Pittsburgh, PA	USA	✓	✓
Shadyside Hospital	Pittsburgh, PA	USA		✓
University of Pittsburgh Medical Center	Pittsburgh, PA	USA	✓	✓
Western Pennsylvania Cancer Institute	Pittsburgh, PA	USA	✓	
Cancer Center of Boston, Plymouth	Plymouth, MA	USA		✓
Legacy Good Samaritan Hospital	Portland, OR	USA		✓
Oregon Health Sciences University (Peds)	Portland, OR	USA	✓	
Oregon Health Sciences University	Portland, OR	USA	✓	✓
Providence Portland Medical Center	Portland, OR	USA		✓
Roger Williams Medical Center	Providence, RI	USA	✓	✓
Cancer & Blood Institute of the Desert	Rancho Mirage, CA	USA		✓
Riverview Medical Center	Red Bank, NJ	USA		✓
Washoe Regional Cancer Center	Reno, NV	USA	✓	✓
Medical College of Virginia	Richmond, VA	USA	✓	✓
University of Rochester Medical Center	Rochester, NY	USA	✓	✓
Mayo Clinic & Foundation	Rochester, MN	USA	✓	✓
Sutter Cancer Center	Sacramento, CA	USA	✓	
Univ of California, Davis Cancer Center	Sacramento, CA	USA	✓	✓
Intermountain Health Care, Inc., LDS Hosp	Salt Lake City, UT	USA	✓	✓
University of Utah Medical Center	Salt Lake City, UT	USA	✓	✓
Univ of Texas, Health Science Center	San Antonio, TX	USA	✓	✓
Wilford Hall Medical Center	San Antonio, TX	USA	✓	
Children's Hospital of San Diego	San Diego, CA	USA		✓

			IBMTR	ABMTR
UC-San Francisco, Moffitt Hosp (Peds)	San Francisco, CA	USA	✓	✓
Mayo Clinic Scottsdale	Scottsdale, AZ	USA	✓	✓
Louisiana State University Medical Ctr	Shreveport, LA	USA	✓	✓
Dakota Midwest Cancer Institute	Sioux Falls, SD	USA		✓
Baystate Medical Center	Springfield, MA	USA		✓
Cardinal Glennon Children's Hospital	St. Louis, MO	USA	✓	✓
St. Louis Children's Hospital	St. Louis, MO	USA	✓	✓
St. Louis Univ Health Sciences Center	St. Louis, MO	USA	✓	✓
Washington Univ School of Medicine	St. Louis, MO	USA	✓	✓
Methodist Hosp & Park Nicollet Cancer Ctr	St. Louis Park, MN	USA		✓
Bennett Cancer Center	Stamford, CT	USA		✓
Stanford University Medical Center	Stanford, CA	USA	✓	✓
University Hosp-SUNY Health Sciences Ctr	Syracuse, NY	USA		✓
H. Lee Moffitt Cancer Center	Tampa, FL	USA	✓	✓
Scott & White Clinic	Temple, TX	USA		✓
St. Vincent Mercy Medical Center	Toledo, OH	USA		✓
University of Arizona Health Science Ctr	Tucson, AZ	USA	✓	✓
St. Francis Hospital	Tulsa, OK	USA	✓	✓
New York Medical College	Valhalla, NY	USA		✓
John Muir Hospital	Walnut Creek, CA	USA		✓
Children's Hospital National Med Center	Washington, DC	USA	✓	
Georgetown University Medical Ctr	Washington, DC	USA	✓	✓
George Washington University Med Center	Washington, DC	USA	✓	✓
Walter Reed Army Medical Center	Washington, DC	USA		✓
Washington Cancer Institute	Washington, DC	USA		✓
Good Samaritan Medical Center	West Palm Beach, FL	USA		✓
Cancer Center of Kansas	Wichita, KS	USA	✓	
North Carolina Baptist Hospital	Winston-Salem, NC	USA	✓	✓
University of Massachusetts Medical Ctr	Worcester, MA	USA	✓	✓
Hospital Central de Valencia	Valencia	Venezuela	✓	

IBMTR / ABMTR
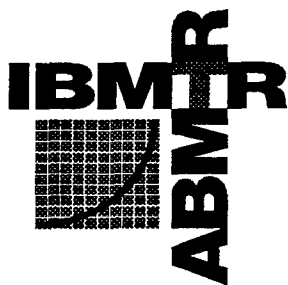
ABMTR Breast Cancer Working Committee

===

Chair:
Karen H. Antman   Columbia University, New York, NY

ABMTR Statistician: Sandy Murphy

Committee:

Martin D. Abeloff	Johns Hopkins Oncology Center, Baltimore, MD
Tauseef Ahmed	New York Medical College, Valhalla, NY
Luke P. Akard	Methodist Hospital of Indiana, Indianapolis, IN
James O. Armitage	University of Nebraska, Omaha, NE
Fikret Arpaci	Gata Military Medical Academy, Ankara, Turkey
Joao L. Ascensao	Univ of Nevada School of Medicine, Reno, NV
Kerry Atkinson	Systemix, Palo Alto, CA
Lois Jeanne Ayash	Univ of Michigan Med Center, Ann Arbor, MI
Murray M. Bern	The Cancer Center of Boston, Boston, MA
Jacob D. Bitran	Lutheran General Hospital Cancer Care Center, Park Ridge, IL
Milan Blaha	Charles University, Hradec Kralove, Czech Republic
Brian J. Bolwell	Cleveland Clinic, Cleveland, OH
Rose Catchatourian	Michael Reese Hospital, Chicago, IL
Takaaki Chou	Niigata Cancer Center Hospital, Niigata, Japan
Neal P. Christiansen	Richland Memorial Hospital / Univ of South Carolina, Columbia, SC
Perry C. Cook	Brooklyn Hospital Ctr, Riverview Medical Ctr, Red Bank, NJ
Edward Alan Copelan	The Ohio State University, Worthington, OH
Antonio De Laurenzi	Ospedale San Camillo, Roma, Italy
Robert L. Drapkin	Morton Plant Hospital, Clearwater, FL
Gerald J. Elfenbein	Univ of South Florida - H Lee Moffitt Cancer Center, Tampa, FL
James L. Gajewski	Univ of Texas - MD Anderson Cancer Center, Houston, TX
Juan J. Garcia	Hospital Privado de Cordoba, Cordoba, Argentina
Stefan Gluck	Northeastern Ontario Regional Cancer Ctr, Sudbury, Ont, Canada
Stuart L. Goldberg	Temple Univ Cancer Center, Philadelphia, PA
Hildegard T. Greinix	University of Vienna, Vienna, Austria
Jean P. Henslee-Downey	University of South Carolina/Richland Memorial Hosp, Columbia, SC
Geoffrey P. Herzig	St. Vincent's Comprehensive Cancer Center, New York, NY
Roger H. Herzig	J. Graham Brown Cancer Ctr, Univ of Louisville, Louisville, KY
Bruce E. Hillner	Virginia Commonwealth University, Richmond, VA
Winston G. Ho	UCI Medical Center, Orange, CA
Osman Ilhan	Univ of Ankara Ibnisina Hospital, Ankara, Turkey
Nalini Janakiraman	Henry Ford Health System, Detroit, MI
Robert A. Joyce	Baptist Medical Center, Jacksonville, FL

Michael John Kennedy	Johns Hopkins Oncology Ctr, Baltimore, MD
Vladimir Koza	Charles University Hospital, Pilsen, Czech Republic
Adrian Langleben	Royal Victoria Hospital, Montreal, Quebec, Canada
Hillard M. Lazarus	Univ Hosp of Cleveland/Case Western Reserve Univ, Cleveland, OH
Edward J. Lee	St. Joseph's Hopsital, Milwaukee, WI
Charles F. LeMaistre	South Texas Cancer Institute, San Antonio, TX
Mark R. Litzow	Mayo Clinic, Rochester, MN
K.M. Steve Lo	Bennett Cancer Center, Stamford, CT
Joseph P. Lynch	West Virginia University, Morgantown, WV
Dipnarine Maharaj	BM/Stem Cell Transplant Inst of Florida, Fort Lauderdale, FL
Kenneth F. Mangan	Temple University, Philadelphia, PA
James R. Mason	Scripps Clinic and Research Institute, La Jolla, CA
Philip L. McCarthy	Roswell Park Cancer Institute, Buffalo, NY
Kenneth R. Meehan	Georgetown University Medical Center, Washington, DC
Rakesh Mehra	MD Anderson Cancer Center, Houston, TX
Letha E. Mills	Dartmouth-Hitchcock Medical Center, Lebanon, NH
Arturo Molina	City of Hope National Medical Center, Duarte, CA
Ahmet Ozet	Gulhane Military Medical Academy, Etlik, Ankara, Turkey
Andrew L. Pecora	North New Jersey Cancer Associates, Hackensack, NJ
Finn Bo Petersen	Univ of Utah Medical Center, Salt Lake City, UT
Gordon L. Phillips	Univ of Kentucky, Markey Cancer Center, Lexington, KY
Donna E. Reece	Univ of Kentucky, Lexington, KY
Elizabeth E. Reed	Univ of Nebraska Medical Ctr, Omaha, NE
Gomez Rodolfo	Universidad de Antioquia, Medellin, Colombia
Ruben A. Saez	H. Lee Moffitt Cancer Center, Tampa, FL
Michael W. Schuster	North Shore University Hospital, Manhasset, NY
Leonard S. Sender	Children's Hospital of Orange County, Orange, CA
Thomas C. Shea	Univ of North Carolina at Chapel Hill, Chapel Hill, NC
Elizabeth J. Shpall	University Hospital, Denver, CO
Barry Skikne	Univ of Kansas Medical Center, Kansas City, KS
Shimon Slavin	Hadassah University Hospital, Jerusalem, Isreal
Gary L. Spitzer	Georgetown University Medical Center, Washington, DC
Edward A. Stadtmauer	Univ of Pennsylvania Hospital, Philadelphia, PA
Martin S. Tallman	Northwestern University Medical School, Chicago, IL
Charles W. Taylor	Univ of Arizona, Tucson, AZ
Robert F. Taylor	St. Luke's Medical Center, Milwaukee, WI
Luen Bik To	Hanson Centre for Cancer Research, Adelaide, Australia
Linda T. Vahdat	Columbia University, New York, NY
Koen W. van Besien	University of Illinois, Chicago, IL
William T. Vaughan	Univ of Alabama at Birmingham, Birmingham, AL
David H. Vesole	Medical College of Wisconsin, Milwaukee, WI
B. Barry Weinberger	LSU Medical Center - Shreveport, Shreveport, LA
Stephanie F. Williams	The Univ of Chicago Medical Center, Chicago, IL
John Reid Wingard	University of Florida, Gainesville, FL
Jane N. Winter	Northwestern University, Chicago, IL
Steven N. Wolff	Vanderbilt University, Nashville, TN

<u>EVALUATION OF PROGRAM</u>
DATA MANAGEMENT WORKSHOP
SCOTTSDALE 1997

<u>SESSION AVERAGE RATING</u>   4.10

<u>HOTEL</u>
GUEST ACCOMODATIONS	3.95
SERVICE	3.88
OTHER	3.63

<u>OVERALL PROGRAM</u>
TOPICS	4.31
SPEAKERS	4.22
SLIDES/OVERHEAD	3.93
HAND-OUTS	4.22

<u>OVERALL VENUE</u>
REGAL MCCORMICK RANCH	4.34
RADISSON RESORT	4.36
MEETING ROOMS	4.18
FOOD & BEVERAGE	4.30

<u>OPENING SESSION OVERVIEW</u>   3.82

<u>DATA MANAGEMENT GENERAL SESSION</u>
INTRODUCTION (MCGARY)	3.98
BASIC STATISTICS (MURPHY)	3.98
DRUG THERAPIES (KOVATOVIC)	3.91
STEMSTOFT DEMO (RACINE)	3.83

<u>WORKSHOPS (2:00-3:30)</u>
TRACK IA	4.33
TRACK IIA	4.56

<u>WORKSHOPS (3:45-5:15)</u>
TRACK IB	4.64
TRACK IIB	3.71

Name (Optional): _____

Social Security Number: __ __ __ - __ __ - __ __ __ __

EVALUATION OF PROGRAM
1997 IBMTR/ABMTR Data Management Workshops
Radisson Resort Scottsdale & Regal McCormick Ranch Resort
Saturday, February 22, 1996 Scottsdale, Arizona

	Poor	Fair	Good	Very Good	Excellent	Comments:
Your Hotel: _____						
Guest accommodations	☐	☐	☐	☐	☐	_____
Service	☐	☐	☐	☐	☐	_____
Other: _____	☐	☐	☐	☐	☐	_____
Overall Program						
Topics	☐	☐	☐	☐	☐	_____
Speakers	☐	☐	☐	☐	☐	_____
Slides/Overheads	☐	☐	☐	☐	☐	_____
Hand-outs	☐	☐	☐	☐	☐	_____
Overall Venue						
Regal McCormick Ranch	☐	☐	☐	☐	☐	_____
Radisson Resort	☐	☐	☐	☐	☐	_____
Meeting Rooms	☐	☐	☐	☐	☐	_____
Food & Beverage	☐	☐	☐	☐	☐	_____
Opening Session: Overview of BMT	☐	☐	☐	☐	☐	_____
Data Management General Session (10:50-12:30PM)						
"Introduction" (McGary)	☐	☐	☐	☐	☐	_____
"Basic Statistics" (Murphy)	☐	☐	☐	☐	☐	_____
"Drug Therapies" (Kovatovic)	☐	☐	☐	☐	☐	_____
"StemSoft Demo" (Racine)	☐	☐	☐	☐	☐	_____
Workshops (2:00-3:30PM)						
Track I: "Registration & Reporting" (Nell/McGary)	☐	☐	☐	☐	☐	_____
Track II: "Reporting Problems" (Knutson)	☐	☐	☐	☐	☐	_____
Workshops (3:45-5:15PM)						
Track I: "Hands-on Reporting" (Knutson)	☐	☐	☐	☐	☐	_____
Track II: "Audit Survival Tactics" (Kabler-Babbitt)	☐	☐	☐	☐	☐	_____

Suggestions for Future Topics: _____

_____

_____

In order to qualify for Category I credit, please complete this form at the conclusion of the program.

Return to Statistical Center by FAX: 414 456-8471, or by mail:
IBMTR/ABMTR, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA

DATA MANAGEMENT $500 GRANT RECIPIENTS

Scottsdale, AZ   February 1997

Bridges, Kerry RN
Richland Memorial Hospital
Columbia, SC

Hazlett, Linda MPH
Richland Memorial Hospital
Columbia, SC

Clayton, Stephanie CRA
Cook Childrens Medical Center
Ft Worth, TX

Hinshaw, Betty RN
UNC Hospitals
Chapel Hill, NC

Daley, Sue
University of Michigan
Ann Arbor, MI

Hoffman, Vicki RN
Columbia Hospital at Medical City Dallas
Dallas, TX

DeFrancisco, Christine CRA
University of California San Diego
La Jolla, CA

Huneke, Norine
Mayo Clinic-Rochester
Rochester, MN

Dillon, Catherine RN, BSN
Riverview Medical Center
Red Bank, NJ

Jenson, Michelle BS
Georgetown University Medical Center
Washington, DC

Dixon, Hope BS
Wayne State University
Detroit, MI

Koerner, Deborah RN
Baptist Medical Center
Jacksonville, FL

Falvey, Mary RN
Roger Williams Medical Center
Providence, RI

Kronish, Lori RN
H Lee Moffitt Cancer Center
Tampa, FL

Fountain, Vernessa ART CTR
Hoag Memorial Hospital/Hoag Cancer Center
Newport Beach, CA

Linder, Tammy BS
University of Rochester Medical Ctr
Rochester, NY

Gray, Priscilla MS
UAMS
Little Rock, AR

Litofsky, Irving SSRA
University of TX, Health Science Center
San Antonio, TX

Griesbach, Donna RN MS CCRC
University of Louisville / Brown Cancer Center
Louisville, KY

Lyons, Rhonda
Shands Hospital/University of Florida
Gainesville, FL

Gyonyor, Eva
Tom Baker Cancer Center
Calgary, Alberta CANADA

Martone, Brenda RN MSN
Loyola University Medical Center
Maywood, IL

Hartley, Eric
Johns Hopkins Oncology Center
Baltimore, MD

McCrae, Jan RN
The Toronto Hospital
Toronto, Ontario CANADA

McIntyre, Wendy RN
St Louis University Health Sciences Center
St Louis, MO

Morris, Mary RN
UNMC
Omaha, NE

Murphy, Juli
Columbia Presbyterian/St Lukes Medical Center
Denver, CO

Nejame, Christine RN
Shands at University of Florida
Gainesville, FL

Nitta, Janet CCHRA (C)
Vancouver Hospital & Health Sciences Center
Vancouver, BC CANADA

Persons, Lori BBA
Northside Hospital/Atlanta Cancer Care
Atlanta, GA

Phlaum, Barbara CCRA (SOCRA)
Cancer & Blood Institute of the Desert
Rancho Mirage, CA

Popovich, Sandra RN
University Hospitals of Cleveland
Cleveland, OH

Randall, Beverly RN
Via Christi Regional Medical Center
Wichita, KS

Reynolds, Deborah RN
Halifax Medical Center
Daytona Beach, FL

Ruehle, Kathleen RN
University of MD Cancer Center
Baltimore, MD

Sapo, Galina
University Hospitals of Cleveland
Cleveland, OH

Sheridan, Mary RN
Medical Center of Delaware
Newark, DE

Sickles, Cheryl BA
University of Penn Cancer Center
Philadelphia, PA

Smith, Peggy RN
Harrington Cancer Center
Amarillo, TX

Stein, Betsy CCRC
Baylor University Medical Center
Dallas, TX

Stevenson, Dustin CRA
UCSD Cancer Center
La Jolla, CA

Tanaka, Leora CRA
UC Davis
Sacramento, CA

Tanczyn, Marjorie MT(ASCP) SBB
Medical Center of Delaware
Newark, DE

Thompson, Clifford
Richland Memorial Hospital
Columbia, SC

Tierney, Kitty RN
Jewish Hospital of Cincinatti
Cincinatti, OH

Tormey, Laura NP
Suny Health Science Center at Syracuse
Syracuse, NY

Tregub, Julie
SHC Specialty Hospital
Westlake Village, CA

Wallace, Corinne RN
St Joseph Hospital
Orange, CA

Weisenborn, Robin MT
West Virginia University
Morgantown, WV

1997 DATA MANAGEMENT WORKSHOP PARTICIPANT LIST

Abraham, Mary RN
Mary Bird Perkins Cancer Center
Clinical Research Dept
4950 Essen Lane
Baton Rouge LA 70809
PHONE: 504 767 0847ext 267
FAX: 504 767 1335

Atkinson, Jeffery
Northwestern University
Bone Marrow Transplant
250 E Superior Ave
Room 1456
Chicago IL 60611
PHONE: 312 908 5400
FAX: 312 908 0478

Biondo, Michael
Washington University Medical School
BMT Dept
660 S Euclid
Box 8117
St Louis MO 63110
PHONE: 314 362 9338
FAX:

Bonvillain, Beth RRA CCRA
Univ of Arkansas for Medical Sciences
CRDM Dept
4301 W Markham St
Slot 724
Little Rock AR 72205
PHONE: 501 686 8274
FAX: 501 296 1466

Bridges, Kerry RN
Richland Memorial Hospital
Div of Transplant Medicine
7 Richland Medical Park
Columbia SC 29203
PHONE: 803 434 4708
FAX: 803 434 3949

Brown, Stanette RN
Richland Memorial Hospital
Div of Transplantation Medicine
7 Richland Medical Park
Columbia SC 27203
PHONE: 803 434 3550
FAX: 803 434 3949

Burch, Ruby
Mayo Clinic Jacksonville
Hematology-Oncology BMT Dept
4500 San Pablo Rd
Jacksonville FL 32224
PHONE: 904 953 7222
FAX: 904 953 2315

Burchett, Sonya BA
Texas Childrens Hospital
Dept of Hematology/Oncology
6621 Fannin MC 3-3320
Houston TX 77030
PHONE: 713 770 4576
FAX: 713 770 4202

Cassar-van der Giessen, Jeannette CRA
Children's Hospital Orange County
Dept of BMT
455 S Main St
Orange CA 92668
PHONE: 714 532 8647
FAX: 714 516 4277

Classen, Sonja RN
Columbia Presby/St Lukes Med Ctr
Dept of BMT
1719 E 19th Ave
Denver CO 80218
PHONE: 303 839 6953
FAX: 303 869 2531

Collison, Sharon
St Lukes Medical Center
Immunotherapy Dept
2900 W Oklahoma Avenue
Milwaukee WI 53221
PHONE: 414 649 5809
FAX: 414 649 7978

Cook, Jennifer CRA
Legacy Good Samaritan Hospital
Cancer Services
1015 NW 22nd Street
Box M230
Portland OR 97210
PHONE: 503 413 7015
FAX: 503 413 6920

Griesbach, Donna RN MS CCRC
University of Louisville / Brown Cancer Center
Dept of BMT
529 S Jackson St
Louisville KY 40202
PHONE: 502 852 5307
FAX: 502 852 4330

Gyonyor, Eva
Tom Baker Cancer Center
BMT Program
1331 29th St NW
Calgary T2N 4N2 Alberta
CANADA
PHONE: 403 670 1752
FAX: 403 283 1651

Hale, Susan RN
University of Utah
BMT Program
50 N Medical Dr SOM 4CA52
Salt Lake City UT 84132
PHONE: 801 585 3229
FAX: 801 585 3432

Hamielec, Mary
University of Wisconsin
Department of Medicine
600 Highland Avenue
Box H4 538CSC
Madison WI 53792
PHONE: 608 263 8629
FAX: 608 262 1982

Harden, Priscilla RN
Childrens Medical Center of Dallas
Center for Cancer & Blood Disorders
1935 Motor Street
Dallas TX 75235-7794
PHONE: 214 640 2765
FAX: 214 640 2095

Hargis, Dana
University of Kentucky
Bone & Marrow Transplant
800 Rose St, Room CC453
Lexington KY 40536
PHONE: 606 323 5015
FAX: 606 323 8990

Hartley, Eric
Johns Hopkins Oncology Center
Dept of Hematologic Malignancies
600 N Wolfe St
Baltimore MD 21287-8985
PHONE: 410 955 8603
FAX: 410 614 9250

Hazlett, Linda MPH
Richland Memorial Hospital
Div of Transplantation Medicine
7 Richland Medical Park
Columbia SC 29203
PHONE: 803 434 4742
FAX: 803 434 3949

Heinsohn, Jean RN
Medical University of So Carolina
Hollings Cancer Center
86 Jonathon Lucas Street
Quad Bldg C, Rm 105
Charleston SC 29425-2802
PHONE: 803 792 8856
FAX: 803 792 1177

Hinshaw, Betty RN
UNC Hospitals
Div of Hematology/Oncology
101 Manning Dr
Chapel Hill NC 27594-7304
PHONE: 919 966 8968
FAX: 919 966 9817

Hoffman, Vicki RN
Columbia Hospital at Medical City Dallas
Stem Cell Transplant
7777 Forest Lane
Bldg A, 12 South
Dallas TX 75230
PHONE: 972 566 3887
FAX: 972 566 3897

Horai, Kim
Scott & White
Cancer Center
2401 S 31st Street
Temple TX 76508
PHONE: 817 724 3879
FAX: 817 724 5890

Lerchie, Susan RN BSN OCN
LSUMC-Shreveport
Dept of Medicine
1501 Kings
Shreveport LA 71130
PHONE: 318 675 5972
FAX: 318 675 6628

Leveque, Gwen RDH
Wayne State University/Karmanus Cancer
Institute
3990 John Rd
Detroit MI 48201
PHONE: 313 745 8484
FAX: 313 993 0967

Linder, Tammy BS
University of Rochester Medical Ctr
BMT/Hematology
601 Elmwood Ave
Box 610
Rochester NY 14642
PHONE: 716 273 4744
FAX: 716 275 5590

Litofsky, Irving SSRA
University of TX, Health Science Center
Dept of Medicine/Hematology
7703 Floyd Curl Dr
San Antonio TX 78284-7880
PHONE: 210 617 5268
FAX: 210 617 5271

Lyons, Rhonda
Shands Hospital/University of Florida
Nursing/BMT Dept
Gainesville FL 32610
PHONE: 352 395 0062
FAX: 352 395 0525

Lyons, Eddy CCRA
Baylor University Medical Center
Blood & Marrow Transplantation
3535 Worth Street, 5th Floor Collins
Dallas TX 75246
PHONE: 214 820 2619
FAX: 214 820 7346

Martone, Brenda RN MSN
Loyola University Medical Center
2160 S First Ave
Bldg 112, Rm 107
Maywood IL 60153
PHONE: 708 327 3228
FAX: 708 327 2210

McCrae, Jan RN
The Toronto Hospital
Dept of Onc ABMT
657 University Ave
Toronto M5G 2C4 Ontario
CANADA
PHONE: 416 340 4800x8546
FAX: 416 340 5087

McIntyre, Wendy RN
St Louis University Health Sciences Center
Dept of BMT Hem Onc
3635 Vista Ave at Grand Blvd
Box 15250
St Louis MO 63110
PHONE: 314 577 8855
FAX: 314 773 1167

McPherson, Jackie
Duke University Medical Center
Pediatric BMT Dept
Erwin St
P o Box 3421
Durham NC 27710
PHONE: 919 681 6382
FAX: 919 681 8151

Minka, Christine
Rocky Mountain Cancer Center
110 E Monroe
Box 7148
Colorado Springs CO 80933-7148
PHONE: 719 577 2555
FAX: 719 577 2553

Miranda, Angela MT, MS
Fairfax Hospital
BMT Unit
3300 Gallows Rd
Falls Church VA 22046
PHONE: 703 698 3280
FAX: 703 698 3657

Phlaum, Barbara
Cancer & Blood Institute of the Desert
Dept of BMT
39700 Bob Hope Dr Ste 108
Rancho Mirage CA 92270
PHONE: 619 568 4461
FAX: 619 568 3617

Popovich, Sandra RN
University Hospitals of Cleveland
Ireland Cancer Center
11100 Euclid Avenue
Cleveland OH 44106
PHONE: 216 844 8303
FAX: 216 844 7855

Ranc, Bette RN
University of MD Cancer Center
Cancer Center
22 South Greene Street
Baltimore MD 21201
PHONE: 410 328 1230
FAX: 410 328 1975

Reynolds, Deborah RN
Halifax Medical Center
Regional Oncology Center/BMT
303 N Clyde Morris Blvd
Daytona Beach FL 32114
PHONE: 904 254 4211
FAX: 904 254 4038

Rogers, Juanita BS
Childrens Hospital of Los Angeles
Dept of BMT
4650 Sunset Blvd
Los Angeles CA 90054
PHONE: 213 669 2218
FAX: 213 660 1904

Rolland-Grinton, Martha RN
The Hospital for Sick Children
Hematology Clinic
555 University Ave
Toronto M5G 1X8 Ontario
CANADA
PHONE: 416 813 7861
FAX: 416 813 8154

Roth, Kathryn RN
Memorial Medical Center
BMT Program
2700 Napoleon Ave
Box 29
New Orleans LA 70115
PHONE: 504 894 2260
FAX: 504 897 4478

Sapozhnikova, Galina
University Hospitals of Cleveland
Ireland Cancer Center
11100 Euclid Avenue
Cleveland OH 44106
PHONE: 216 844 8376
FAX: 216 844 8599

Satarino, Joyce CRA
University of Michigan
Dept of Pediatrics
1500 E Medical Drive
Box 0238
Ann Arbor MI 48109
PHONE: 313 763 6344
FAX: 313 936 8520

Schweichler, Louis
Arlington Cancer Center
BMT Dept
906 W Randol Mill Rd
Arlington TX 76012-6509
PHONE: 817 261 4906
FAX: 817 261 9623

Scott, Kathleen CRA,CTR
Childrens Hospital of San Diego
Division of Hematology/Oncology
3020 Childrens Way/MC 5035
San Diego 92123-4282 CA 92123-4282
PHONE: 619 576 5983
FAX: 619 495 8533

Sexauer, Chris RN
Baptist Regional Cancer Institute
Peripheral Stem Cell Program
1235 San Marco Blvd, Suite 3
Jacksonville FL 32207
PHONE: 904 202 7009
FAX: 904 202 7227

Tierney, Kitty RN
Jewish Hospital of Cincinatti
BMT Program
3200 Burnet Ave
Cincinatti OH 45229
PHONE: 513 569 2696
FAX: 513 569 2527

Tregub, Julie
SHC Specialty Hospital
BMT Program
4415 S Lakeview Cyn Rd
Westlake Village CA 91361
PHONE: 818 865 4445
FAX: 818 865 4413

Vachon, Marie-France RN CRA
Hopital Ste Justine
2nd Block 4
3175 Cote Ste Catherine
Montreal H3T 1C5 Quebec
CANADA
PHONE: 514 345 4969
FAX: 514 345 4792

Vadeboncoeur, Renee RN
University of Utah
Div of Hematology/Oncology
50 N Medical Dr
Salt Lake City UT 84132
PHONE: 801 585 3229
FAX: 801 585 3432

Wallace, Corinne RN
St Joseph Hospital
Cancer Center
1100 W Stewart Dr
Orange CA 92668
PHONE: 714 771 8999
FAX: 714 744 8592

Weisenborn, Robin MT
West Virginia University
BMT Program
Medical Center Drive
Box 9162
Morgantown WV 26506
PHONE: 304 293 6859
FAX: 304 293 2134

Westcott, Dana
Harris Methodist Fort Worth
Out-patient BMT
1300 W Terrell
Fort Worth TX 76104
PHONE: 817 820 4912
FAX: 817 820 4991

Williams, Lori RN
American Oncology Resources
Planning and Development
16825 Northchase Dr, Suite 1300
Houston TX 77060
PHONE: 713 775 0186
FAX: 713 775 0386

Winter, Rita
Via Christi Regional Medical Center-St Francis
Campus
Oncology Services
929 North St Francis
Wichita KS 67214
PHONE: 316 268 5868
FAX: 316 291 7855

Zeswitz, Jill
Memorial Medical College
BMT Program
2700 Napoleon Ave
New Orleans LA 70115
PHONE: 504 897 4229
FAX: 504 897 4478

IBMTR ABMTR

1997 Annual Participants' Meeting

February 22-25

Radisson Resort Scottsdale
Scottsdale, Arizona, USA
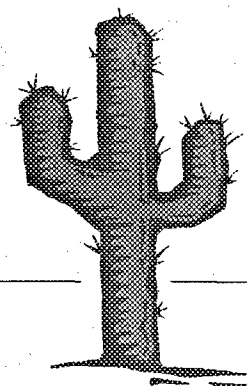
Supported by educational grants from:

♦ Amgen, Inc.   ♦ Baxter Healthcare, Inc., Biotech Group
♦ BIS Laboratories   ♦ Bristol-Myers Oncology   ♦ Cell Therapeutics, Inc.
♦ CellPro, Inc.   ♦ Centeon   ♦ Chiron Therapeutics   ♦ COBE BCT, Inc.
♦ Immunex Corporation   ♦ Janssen Pharmaceutica   ♦ Life Technologies, Inc.
♦ The Liposome Company, Inc.   ♦ NCGS and Associates, Inc.
♦ NeXstar Pharmaceuticals, Inc.   ♦ Ortho Biotech   ♦ Pfizer, Inc.
♦ Pharmacia & Upjohn, Inc.   ♦ QLT PhotoTherapeutics, Inc.
♦ Quantum Health Resources   ♦ Roche Laboratories   ♦ Sandoz Oncology
♦ StemCell Technologies, Inc.   ♦ SyStemix   ♦ Wyeth-Ayerst Laboratories

MEDICAL COLLEGE OF WISCONSIN

CME program
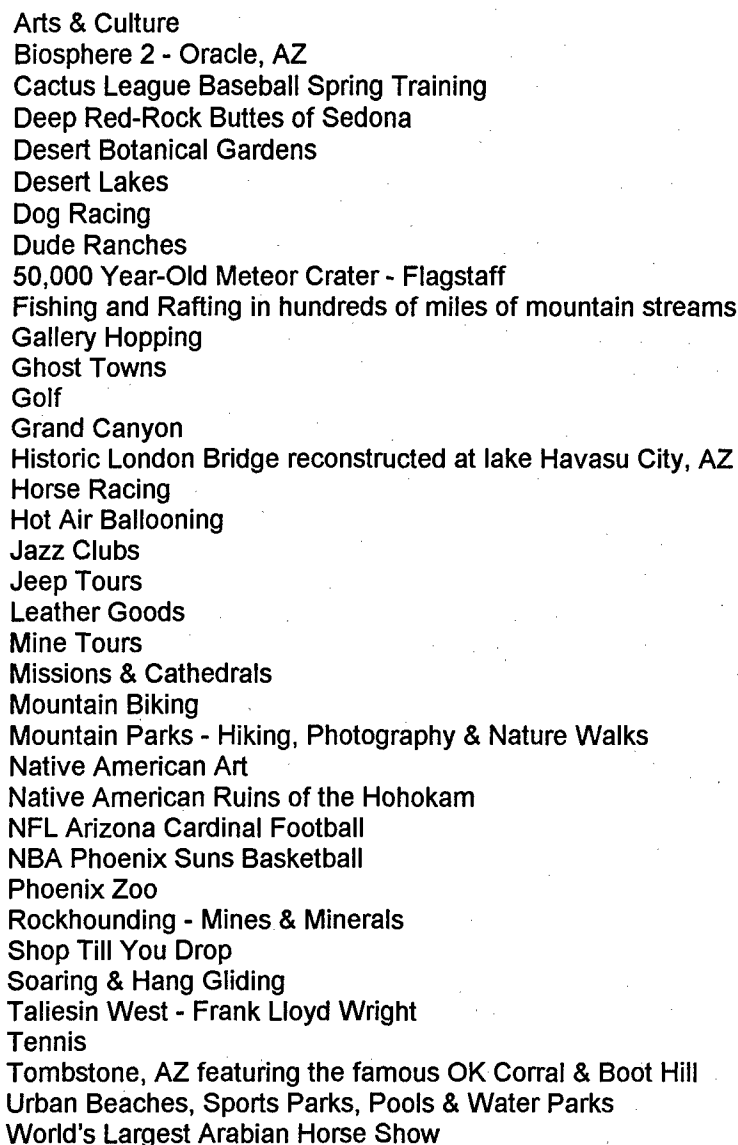
Continuing Medical Education credits available through the Medical College of Wisconsin

The Radisson Resort Scottsdale is located just minutes from Phoenix, Arizona in the breathtaking Sonoran Desert.
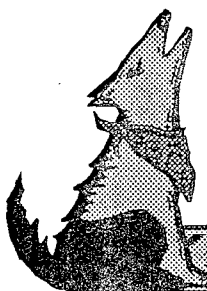
...But We Can't *Ski* in Scottsdale!!!

Right.

Arts & Culture
Biosphere 2 - Oracle, AZ
Cactus League Baseball Spring Training
Deep Red-Rock Buttes of Sedona
Desert Botanical Gardens
Desert Lakes
Dog Racing
Dude Ranches
50,000 Year-Old Meteor Crater - Flagstaff
Fishing and Rafting in hundreds of miles of mountain streams
Gallery Hopping
Ghost Towns
Golf
Grand Canyon
Historic London Bridge reconstructed at lake Havasu City, AZ
Horse Racing
Hot Air Ballooning
Jazz Clubs
Jeep Tours
Leather Goods
Mine Tours
Missions & Cathedrals
Mountain Biking
Mountain Parks - Hiking, Photography & Nature Walks
Native American Art
Native American Ruins of the Hohokam
NFL Arizona Cardinal Football
NBA Phoenix Suns Basketball
Phoenix Zoo
Rockhounding - Mines & Minerals
Shop Till You Drop
Soaring & Hang Gliding
Taliesin West - Frank Lloyd Wright
Tennis
Tombstone, AZ featuring the famous OK Corral & Boot Hill
Urban Beaches, Sports Parks, Pools & Water Parks
World's Largest Arabian Horse Show

- See You Again in Keystone in 1998 -

The IBMTR/ABMTR research program

25 Years of International Scientific Collaboration

IBMTR/ABMTR members can be proud of many accomplishments stemming from more than 25 years of research in blood and marrow transplantation. Established in the early 1970's, the IBMTR/ABMTR today is firmly rooted in the global community of blood and marrow transplant research.

During his 20+ year tenure with the Statistical Center, founding director Mortimer M. Bortin, MD, often attributed the Registries' success to *"a spirit of international scientific collaboration"*. This spirit continues to be shared by hundreds of transplant institutions around the world, enabling a research effort addressing important issues in blood and marrow transplantation, and establishing the Registries as a vital resource for scientists, clinicians, patients and others involved in cancer treatment.

More than 400 participating centers

Allogeneic and autologous blood and marrow transplant data are contributed to the IBMTR/ABMTR Statistical Center by more than 400 participating centers, worldwide. The IBMTR/ABMTR research program depends on these important contributions of time and effort.

Active participation continues in Scottsdale, February '97

Our goal for 1997 is to have each contributing team represented at the joint IBMTR/ABMTR Annual Participants' Meeting at the Radisson Resort Scottsdale.

We enthusiastically welcome attendance by senior and junior faculty members, clinical research associates and data managers, nursing staff and other allied health professionals. Team members' active participation in specific areas of interest and expertise add greatly to the overall program. Participants will play an active role in planning the Registries' scientific agenda.

Non-members are also welcome to take advantage of this opportunity to learn about Registry activities and participate in the scientific program.

1997 Annual Participants' Meeting
February 22-25
Radisson Resort Scottsdale, Arizona, USA
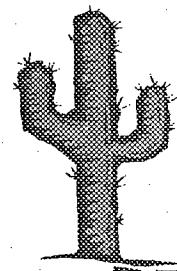
For Meeting Information call: 414-456-8377 or fax: 414-266-8471   For Housing call: 602-991-3800

Why you should attend the 1997 Participants' Meeting

1997 Participants' Meeting in the Valley of the Sun — Scottsdale,AZ — February 22-25

Meeting Objectives

♦ to review the "state of the art" in blood and marrow transplantation;

♦ to review Registry accomplishments during the past year;

♦ to discuss the progress of current studies and plan future scientific studies;

♦ to provide educational sessions for data managers, nurses and other allied health professionals working in blood and marrow transplantation.
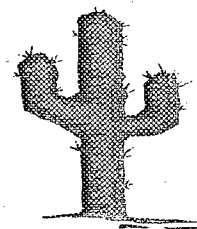
Working Committee Meetings

IBMTR and ABMTR disease- and treatment-specific Working Committees are open to all interested in taking an *ACTIVE* role in ongoing and future studies. *All Working Committee members should plan to attend.*

Working Committees will review the past year's accomplishments, discuss current studies and plan future studies. Participation in these meetings is an opportunity to help determine the Registries' scientific agenda and discuss use of the Registries' extensive databases.

1997 IBMTR & ABMTR Working Committees

IBMTR
Acute Leukemia
CLL, Lymphoma & Multiple Myeloma
Chronic Myelogenous Leukemia
GVH/GVL, Immune Reconstitution
Histocompatibility, Alternative Donors
   & Alternative Stem Cell Sources
Immune Deficiencies & Metabolic Diseases
Late Effects
Severe Aplastic Anemia

ABMTR
Breast Cancer
Leukemia
Lymphoma
Multiple Myeloma
Ovarian Cancer
Pediatric Cancer

For Meeting Information call: 414-456-8377 or fax: 414-266-8471   For Housing call: 602-991-3800

Housing & Accommodations

Reservations Worldwide ☎ *800-333-3333   Housing Form Due: January 1*

A limited number of sleeping rooms at special conference rates of $159 single or $169 double occupancy are reserved for IBMTR/ABMTR Meeting participants. The rates are available for 3 days before and after the conference for those wishing to extend their February stay in the picturesque "Valley of the Sun". Take advantage of these special room rates, which represent *substantial* discounts during peak season for Scottsdale-area resorts.

Please complete the enclosed Housing Form and return it directly to the Radisson Resort Scottsdale **prior to January 1, 1997**. It is strongly recommended that reservations be made **early,** as accommodations will be difficult and more costly to obtain after the January 1 housing deadline. Please indicate a major credit card number for a one-night deposit. Reservations will not be held without a deposit. Reservations made after the deadline may not be available at the discounted conference rate and last minute requests may be impossible to accommodate.

RADISSON RESORT SCOTTSDALE
ROOM RATES PER NIGHT
Standard rooms $159 single and $169 double
Suites $250
subject to availability

Cancellation: Call the Hotel directly to cancel housing reservations. No shows, late arrivals and early departures will be charged the full room rate for the entire reserved period. **THE IBMTR/ABMTR WILL NOT BE HELD RESPONSIBLE FOR HOUSING CANCELLATIONS OR "NO SHOWS". HOUSING IS THE INDIVIDUAL RESPONSIBILITY OF EACH MEETING PARTICIPANT.**

Poster Sessions Combined with Evening Receptions

Each late afternoon poster session will be combined with a hosted reception featuring The Radisson Resort Scottsdale's award-winning light buffet-style cuisine and beverages.

A $500 investigator award will be given for the best abstract submitted, as determined by Working Committee Chairs.
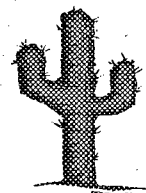
Abstract Instructions   Submission Deadline: November 15, 1996

1. Abstract must be typed on the enclosed ABSTRACT FORM.

2. CAPITALIZE entire title and UNDERSCORE author's names (underscoring or capitalizing for emphasis in text is unacceptable. Single space all typing (no space between title and body or between paragraphs). Indent each paragraph three spaces. Do not indent title. Draw special symbols in black ink.

3. Please do not reduce the abstract on a photocopy machine! Type abstract in 12 point type or larger. Abstracts submitted in a reduced format may not be included in the Abstract Book. Abstracts must be received by November 15, 1996 to ensure publication in the Abstract Book. ABSTRACT WILL APPEAR EXACTLY AS SUBMITTED. Smudges, errors, misspellings, faint type, etc. should be avoided.

4. Make the TITLE brief, clearly indicating the nature of the investigation. After the title, list the authors' names and institutional affiliations. Omit degrees, titles, institutional appointments, street addresses and zip or postal code.

5. Organize the body of the abstract as follows:

   - A statement of the purpose of the study (preferably one sentence)
   - A statement of the methods used
   - A summary of the results presented in sufficient detail to support the conclusions
   - A statement of conclusions reached. It is not satisfactory to state, "The results will be discussed" or "Other data will be presented.
   - Do not use subtitles, e.g., "Methods" or "Results".

6. Simple tables or graphs, neat and in black ink, may be included if they fit within the Abstract Form.

7. Abbreviations must be defined by placing them in parentheses after the full word the first time they appear. Use numerals to indicate numbers except when beginning sentences.

8. The material must be in camera-ready form, i.e., type must be laser quality, 300 dpi or better (no dot matrix). USE BLACK INK. Practice fitting text into the Abstract Form.

9. NO abstract may be presented if previously presented orally at a national or international meeting.

10. **Submit abstract (original plus 4 copies) BEFORE NOVEMBER 15, 1996.**

For Meeting Information call: 414-456-8377 or fax: 414-266-8471   For Housing call: 602-991-3800

Abstract Form   IBMTR/ABMTR 1997

1997 Annual Participants' Meeting
February 22-25
Radisson Resort Scottsdale, Arizona, USA
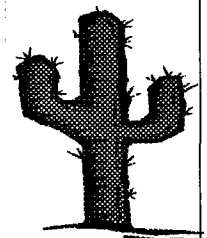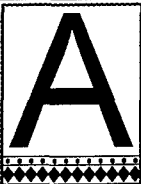
Abstract submission information
Questions? call 414-456-8377

please type or print

PERSON TO NOTIFY OF ABSTRACT ACCEPTANCE:

Name _____

Institution_____

Address_____

City/State/Country_____

Telephone_____

FAX_____

ABSTRACT WILL BE PRESENTED BY: ☐ *check here if same as above*

Name_____

Institution_____

Telephone_____

FAX_____

☐ Allogeneic
☐ Autologous
☐ Acute Leukemia
☐ Breast Cancer
☐ Chronic Leukemia
☐ GVH/GVL
☐ Histocompatibility/Alternative Stem Cell Sources
☐ Immune Deficiencies/ Metabolic Diseases
☐ Late Effects
☐ Lymphoma
☐ Multiple Myeloma
☐ Ovarian Cancer
☐ Pediatric Cancer

> **Abstract Deadline:**
> **November 15, 1996**

The presenter and authors must identify any financial interests in products or processes involved in their research. This includes stock ownership, membership on an advisory board or board of directors, corporate-sponsored research, or other substantive relationships. (If none, write "none". If left blank, the interpretation will be "none".)

DISCLOSURE STATEMENT: _____

_____

IBMTR/ABMTR - 1997 Annual Participants' Meeting - February 22-25

MEETING REGISTRATION FORM

Return 2-page Registration Form to D'Etta Waldoch Koser, CMP at IBMTR/ABMTR Statistical Center by FAX: 414-266-8471
or by mail: IBMTR/ABMTR, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI, 53226, USA

FIRST NAME_____ MIDDLE_____

LAST (FAMILY) NAME_____

  please check: ☐ MD   ☐ PhD   ☐ RN   ☐ Other, specify:_____

TITLE_____

INSTITUTION_____

DEPARTMENT_____ POST BOX/MAIL STOP_____

STREET ADDRESS_____

CITY_____ STATE_____

ZIP/POSTAL CODE_____ COUNTRY_____

TELEPHONE [_____] _____ FAX [_____] _____

IBMTR TEAM # __ __ __   IBMTR TEAM LEADER:_____

ABMTR TEAM # __ __ __   ABMTR TEAM LEADER:_____

DATE OF ARRIVAL February _____, 1997   **ANTICIPATED DEPARTURE** February _____, 1997

  ☐ Check here if you have any needs/disabilities for which you require special accommodation and we will contact you.

CREDIT FOR ATTENDANCE   Certificates of attendance are available. Physicians requesting continuing medical education (CME) credits, or allied health professionals requesting continuing education units (CEU) must include social security number.

☐ CME credit requested (MD's only)   ☐ CEU credit requested   ☐ Certificate of attendance requested

  Social Security Number (REQUIRED FOR CME/CEU CREDIT): ____ ____ ____ - ____ ____ - ____ ____ ____ ____

REGISTRATION FEES & METHOD OF PAYMENT   PAYMENT IS DUE WITH REGISTRATION FORM

	before Nov 1	before Dec 1	on or after Dec 1
IBMTR/ABMTR Team Members			
MD/PhD	$300	$375	$425
Data Mgr./Nurse or other afflied health professionals	$ 75	$100	$125
Corporate Members	$400	$500	$600
Non-Members	$500	$600	$700

Enclosed is check #_____ in the amount of US $_____, made payable to **Medical College of Wisconsin**
(print participant's name on check). International funds must be in US dollars; credit cards are processed in US dollars and are subject to current exchange rates.)

Charge to: ☐ MasterCard® 16 digits   ☐ VISA® 13 or 16 digits   Expiration:____ ____ / ____ ____

                                                                          month / year

Card Number: ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___

Signature of Cardholder:_____
Print Cardholder's name:_____

IBMTR/ABMTR - 1997 Annual Participants' Meeting - February 22-25

SIMULTANEOUS SESSIONS PREFERENCES

Return to D'Etta Waldoch Koser, CMP at IBMTR/ABMTR Statistical Center by FAX: 414-266-8471
or by mail: IBMTR/ABMTR, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI, 53226, USA

FIRST NAME_____

LAST (FAMILY) NAME_____

PLEASE INDICATE BELOW WHICH OF THE SIMULTANEOUS SESSIONS YOU PLAN TO ATTEND (CHECK ONE BOX PER TIME PERIOD) AND RETURN THIS PAGE WITH REGISTRATION FORM. TIMES OF SESSIONS ARE TENTATIVE AND SUBJECT TO CHANGE.

SATURDAY, FEBRUARY 22

10:20-12 NOON
☐ **Scientific Session I: Stem Cell Sources**
☐ ABMTR Pediatric Cancers Working Committee   ☐ Data Management Overview
☐ IBMTR/ABMTR CLL Working Committee

1:45-3:15 PM
☐ **Scientific Session II: Graft Engineering/ Minimal Residual Disease**
☐ IBMTR GVH/GVL & Immune Reconstitution Working Committee   ☐ Data Management Track I
☐ IBMTR Late Effects   ☐ Data Management Track II

3:35-5:00 PM
☐ **Scientific Session III: Transplants for Leukemia**
☐ IBMTR Histocompatibility, Alt Donors, etc. Working Committee   ☐ Data Management Track I
☐ ABMTR Ovarian Cancer Working Committee   ☐ Data Management Track II

SUNDAY, FEBRUARY 23

9:00-10:30 AM
☐ **Scientific Session IV: Transplants for Aplastic Anemia & Other Non-Malignant Marrow Disorders**
☐ IBMTR Metabolic Diseases & Immune Deficiencies Working Committee

10:50-12:30 PM
☐ **Scientific Session V: Transplants for Lymphoma & CLL**
☐ IBMTR/ABMTR Acute Leukemia Working Committee

6:45-8:15 PM
☐ **Scientific Session VI: Late Effects/Quality of Life**
☐ IBMTR CML Working Committee

MONDAY, FEBRUARY 24

9:00-10:30 AM
☐ **Scientific Session VII: Transplants for Solid Tumors**
☐ IBMTR/ABMTR Lymphoma Working Committee

10:50-12:30 PM
☐ **Scientific Session VIII: GVL/GVH**
☐ ABMTR Breast Cancer
☐ IBMTR SAA

IBMTR/ABMTR - 1997 Data Management Workshops - February 22

$500 GRANT APPLICATION

IMPORTANT: Return this Application with your completed Registration Form and credit card information
DEADLINE: NOVEMBER 1, 1996

to: D'Etta Waldoch Koser, CMP at IBMTR/ABMTR Statistical Center by FAX: 414-266-8471
or by mail: IBMTR/ABMTR, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI, 53226, USA

ELIGIBILITY

Does your team currently report autotransplants for breast cancer to the ABMTR, or plan to?

☐ Yes, we currently report autotransplants for breast cancer

☐ We are planning to start reporting autotransplants for breast cancer   (indicated date anticipated:___/___/___)

☐ No (indicate reason):_____

NOTE: Each applicant must submit a separate Grant Application & Registration Form

FIRST NAME_____

LAST (FAMILY) NAME_____

   please check: ☐ MD   ☐ PhD   ☐ RN   ☐ Other, specify:_____

TITLE_____

INSTITUTION_____

TELEPHONE [_____] _____

FAX [_____] _____

SOCIAL SECURITY NUMBER (IF US CITIZEN): ___ ___ ___-___ ___-___ ___ ___ ___

IBMTR TEAM # ___ ___ ___   IBMTR TEAM LEADER_____

ABMTR TEAM # ___ ___ ___   ABMTR TEAM LEADER_____

IBMTR/ABMTR - 1997 Annual Participants' Meeting - February 22-25
RADISSON RESORT SCOTTSDALE
ROOM RESERVATION FORM

The Radisson Resort Scottsdale is pleased you have chosen us for your upcoming visit. Our staff looks forward to having you as our guest. In making your reservation we request that you either:

1) Enclose a check or money order covering the first night's stay; or
2) Send us the entire number of your credit card. We accept: **American Express, Diners Club, VISA, MasterCard, Carte Blanche or Discover.** Please include the expiration date and your signature.

Standard Rooms $159 single or $169 double — Suites $250
Please complete this form and return prior to: JANUARY 1, 1997
Reservations requested after the above cut-off date are subject to availability

The Radisson Resort Scottsdale
☎ 601-991-3800; reservations worldwide: 800-333-3333; fax: 602-948-1381
7171 North Scottsdale Road, Scottsdale, AZ, 85253-3696, USA

CANCELLATIONS: Call the Radisson directly to cancel housing reservations. No shows, late arrivals and early departures will charged the full room rate for the entire reserved period. Housing is the responsibility of each meeting participant. The IBMTR/ABMTR will not be held responsible for housing cancellations.

FIRST NAME_____

LAST (FAMILY) NAME_____

INSTITUTION_____

POST BOX/MAIL STOP_____

STREET ADDRESS_____

CITY_____ STATE_____

ZIP/POSTAL CODE_____ COUNTRY_____

TELEPHONE [_____] _____ FAX [_____] _____

DATE OF ARRIVAL: February_____, 1997   DATE OF DEPARTURE: February_____, 1997
☐ Check here if you have any needs/disabilities for which you require special accommodation and we will contact you.

PLEASE RESERVE_____ROOMS FOR_____PEOPLE.   ☐ SMOKING   ☐ NON-SMOKING
NAME OF PERSON(S) SHARING ACCOMMODATIONS:

_____

I authorize The Radisson Resort Scottsdale to charge my account for one night's deposit and all applicable taxes. Check-out time is 12 NOON. Rooms may not be available for check-in until after 4 PM. Please apply 10.725% room tax to above rates (tax rate subject to change).

☐ Check or money order enclosed   ☐ Diners Club   ☐ MasterCard   ☐ Carte Blanche
☐ American Express   ☐ Discover   ☐ VISA

Card Number: __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __   Expiration: __ __ / __ __

Signature of cardholder:_____

Printer cardholder's name:_____

R egistration Information

Meeting registration is easy by fax!   Do it today!

Complete the enclosed Registration Form, including your VISA or MasterCard number, and fax to the Statistical Center at 414-266-8471. Checks, made payable to The Medical College of Wisconsin, may be mailed to the Statistical Center. We regret that we cannot accept American Express for meeting registration fees. International funds must be submitted in US Dollars. All credit cards are processed in US Dollars and are subject to current exchange rates.

Registration Forms received prior to November 1 qualify for the preregistration discount. Those received on or after December 1 must pay the full conference rate, as indicated. Payment is due with Registration Form.

Registration fees include admission to all sessions and exhibits, all IBMTR/ABMTR conference materials, abstract book and program, breakfast, coffee breaks and refreshments, and evening poster session receptions. Confirmation for each registered participant will be returned by fax.

1997 IBMTR/ABMTR MEETING REGISTRATION FEES			
	before Nov 1	before Dec 1	on or after Dec 1
PARTICIPATING TEAM MEMBERS			
MD/PhD	$300	$375	$425
Allied Health Professionals* from Participating Teams and Accompanying Persons	$75	$100	$125
CORPORATE MEMBERS	$400	$500	$600
NON-MEMBERS	$500	$600	$700

***Data Management Grants:** A limited number of $500 grants are available on a first-come, first-serve basis to data management personnel attending the Data Management Workshops on Saturday, February 22. To be eligible, data managers must be from centers currently reporting, or planning to report, autotransplants for breast cancer to the ABMTR. The enclosed application form must be returned to the Statistical Center prior to November 1, 1996 for consideration. Additional details may be found on the enclosed application. For more information contact D'Etta Waldoch Koser, CMP, Associate Director-International Programs at the Statistical Center at: 414-456-8377.

Cancellation: Meeting registration is fully refundable until November 30. All cancellations must be made in writing and may be faxed to the Statistical Center at 414-266-8471. Cancellations made on or after December 1 will be assessed a non-refundable handling fee of US $25.00; On January 1 the cancellation fee will increase to US $50.00.

1997 Annual Participants' Meeting
February 22-25
Radisson Resort Scottsdale, Arizona, USA

Data Management Workshops

Featuring 2 Learning Tracks...   Saturday, February 22, 1997

Due to enthusiastic feedback from participating IBMTR and ABMTR data management professionals, we are pleased to offer a full day of Data Management Workshops at the 1997 Annual IBMTR/ABMTR Participants' Meeting. Data managers, clinical research associates and research nurses will find topics of interest and direct communication with on-site Statistical Center staff members leading informal, participatory Workshops on two tracks. Both tracks will discuss recent changes in IBMTR/ABMTR Registration and Reporting procedures.

TRACK I   features fundamental concepts for those attending the Workshops for the first time

TRACK II   designed for more experienced data management and nursing professionals, features special topics related to clinical research and audit management

Additionally, StemCell Technologies, Inc. will demonstrate *StemSoft®* software and their interrelated statistical analysis package. "Hands-on" training is available on Sunday, February 23 for those who preregister with StemCell Technologies, Inc. (details below). Data management personnel are invited to stay for the entire 4-day meeting.

$500 Grants for Data Management Workshops

The Statistical Center was awarded a grant from the US Department of Defense which allows us to provide 50 data managers with $500 each to offset some of the travel costs associated with attending the 1997 Workshops. To be eligible, data managers must be from centers currently reporting, or planning to report autotransplants for breast cancer to the ABMTR.

Grants are awarded as they are received, with priority given to first-time attendees. Please complete the enclosed Grant Application Form and return with your completed Registration Form as soon as possible.

Deadline for Grant Application submission is November 1, 1996. *Grant awards go fast — do not delay!*

StemCell Technologies, Inc.

StemCell Technologies, Inc. will present a one-day hands-on training session for their StemSoft line of products on Sunday, February 23. Programs covered in the course will include:

BMTbase 095-Reports - a database to facilitate data entry and reporting to IBMTR/ABMTR
BMTbase 095-Registration - the IBMTR/ABMTR initial reporting form
BMTstats - statistical analysis program with the capabilities to produce Kaplan-Meier curves
BMTtransfer - program for 095-Reports data submission to IBMTR/ABMTR
BMTmerge - remote data exchange program

Data Managers and all 'end-users' of StemSoft software who want to achieve greater levels of performance and effectiveness with the software will benefit from this session. The fee for attending this session is $300 US. To register, please contact Violet Molnar at StemCell Technologies, Inc. at 604-877-0713.

Continuing Medical Education

The Medical College of Wisconsin (MCW) is accredited by the US Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. MCW designates this continuing medical education (CME) activity for credit in Category I of the Physician's Recognition Award of the American Medical Association for the 1997 Annual IBMTR/ABMTR Participants' Meeting. MCW, accredited by the Council on the Continuing Education Unit, certifies that this program meets the criteria for Continuing Education Units (CEU). Participants requesting either CME or CEU credit should check the appropriate box on the enclosed Registration Form and must include social security number.

CME/CEU Disclosure

The Statistical Center of the IBMTR and ABMTR is committed to providing unbiased, balanced and objective educational and scientific programs. In accordance with ACCME guidelines, all 1997 Annual Meeting speakers are asked to provide relevant disclosure statements, which are on file at the Medical College of Wisconsin Continuing Medical Education office.

Travel Assistance

Hertz - the official car rental company

Hertz has been appointed the official car rental company for the 1997 IBMTR/ABMTR Participants' Meeting in Scottsdale, Arizona, February 22-25. Special discount rates, with free unlimited mileage are guaranteed one week before and one week after the IBMTR/ABMTR meeting dates, subject to car availability. At the time of reservation booking, these rates will automatically be compared to Hertz published rates, assuring meeting participants are quoted the best comparable rates. Rates are available from Phoenix, Scottsdale and Tucson, Arizona. Standard rental conditions and qualifications apply, including minimum rental age. Check with your Hertz representative for further details.

> For reservations, call Hertz at 1-800-654-2240 in the US, in Canada at 1-800-263-0600, or check with your travel agent. Refer to CV#17584.

Meetings & Incentives - air transportation to Phoenix, AZ

Special air transportation packages are available through *Meetings & Incentives*, independent specialists in medical conferences worldwide. Discounts are provided on super saver, full coach or first class. Please identify yourself as an IBMTR/ABMTR Scottsdale Meeting Participant. Discounted tickets are limited in availability and carry penalties once issued. Wherever possible, seat assignments and boarding cards will be issued per participant's preference.

> For reservations, call *Meetings & Incentives* at 1-800-776-3582 ext. 126 or 414-835-3553 ext. 126; fax: 414-835-3569.

For Meeting Information call: 414-456-8377 or fax: 414-266-8471   For Housing call: 602-991-3800

PROVISIONAL AGENDA-AT-A-GLANCE

SATURDAY - FEBRUARY 22

7:00AM-8:30AM
BREAKFAST & REGISTRATION

8:30AM-10:00AM
OPENING GENERAL SESSION
Welcome
IBMTR Update
ABMTR Update
Selected Studies in Progress

10:00AM-10:20AM
BREAK & EXHIBITS

10:20AM-12:00N
SCIENTIFIC SESSION I
Stem Cell Sources

WORKING COMMITTEE MEETINGS
ABMTR Pediatric Cancers
IBMTR/ABMTR Chronic Lymphocytic Leukemia

DATA MANAGEMENT WORKSHOPS
Introduction to IBMTR/ABMTR Data Management
Basic Statistics
Drug Therapies
StemSoft Products Demonstration

12:00N-1:30PM
LUNCHEON

OPENING: KEYNOTE ADDRESS
        TBA

1:45PM-3:15PM
SCIENTIFIC SESSION II
Graft Engineering / Minimal Residual Disease

WORKING COMMITTEES
IBMTR GVH/GVL & Immune Reconstitution
IBMTR Late Effects

DATA MANAGEMENT
Track I: Basic Registration & Reporting
Track II: Problems in Reporting

3:15PM-3:35PM
BREAK & EXHIBITS

3:35PM-5:00PM
SCIENTIFIC SESSION III
Transplants for Leukemia

WORKING COMMITTEES
IBMTR Histocompatibility, Alternative Donors & Stem Cell Sources
ABMTR Ovarian Cancer

DATA MANAGEMENT
Track I: Hands-on Reporting
*Track II:*Audit Survival Tactics

5:30PM-6:45PM
EVENING OPENING RECEPTION
EXHIBITS & BUFFET

SUNDAY - FEBRUARY 23

8:00AM-9:00AM
BREAKFAST & REGISTRATION

9:00AM-10:30AM
SCIENTIFIC SESSION IV
Transplants for Aplastic Anemia &
Other Non-Malignant Marrow Disorders

WORKING COMMITTEE MEETINGS
IBMTR Metabolic Diseases & Immune Deficiencies
IBMTR/ABMTR Multiple Myeloma

10:30AM-10:50AM
BREAK & EXHIBITS

10:50AM-12:30PM
SCIENTIFIC SESSION V
Transplants for Lymphoma &
Chronic Lymphocytic Leukemia

WORKING COMMITTEE MEETING
IBMTR/ABMTR Acute Leukemia

12:30PM-2:30PM
AFTERNOON
AVAILABLE
FOR
RECREATIONAL
ACTIVITIES

IBMTR EXECUTIVE
COMMITTEE

3:30PM-5:30PM

IBMTR ADVISORY
COMMITTEE

5:00PM-6:45PM
EVENING RECEPTION
EXHIBITS & BUFFET
POSTER SESSION 1

6:45PM-8:15PM
SCIENTIFIC SESSION VI
Late Effects/Quality of Life

WORKING COMMITTEES
IBMTR Chronic Myelogenous Leukemia

StemCell Technologies, Inc.
Full-day hands-on training session for StemSoft products on
Sunday, February 23; more information available on page 8.

PROVISIONAL AGENDA-AT-A-GLANCE

MONDAY - FEBRUARY 24

Time	Event
7:00AM-	**BREAKFAST & REGISTRATION**
8:00AM-9:00AM	**BUSINESS MEETING**
9:00AM-10:30AM	**SCIENTIFIC SESSION VII** Transplants for Solid Tumors
	WORKING COMMITTEE MEETING IBMTR/ABMTR Lymphomas
10:30AM-10:50AM	**BREAK & EXHIBITS**
10:50AM-12:30PM	**SCIENTIFIC SESSION VIII** GVL/GVH
	WORKING COMMITTEES ABMTR Breast Cancer IBMTR Severe Aplastic Anemia
12:30PM-2:30PM	**ABMTR EXECUTIVE COMMITTEE**
3:30PM-5:30PM	**ABMTR ADVISORY COMMITTEE**
5:30PM-6:45PM	**EVENING RECEPTION EXHIBITS & BUFFET** **POSTER SESSION 2 - BEST POSTER AWARD**
6:45PM-8:15PM	**SCIENTIFIC SESSION IX** Alternative Donor Transplants (unrelated and HLA-mismatched related donors)

AFTERNOON AVAILABLE FOR RECREATIONAL ACTIVITIES

TUESDAY - FEBRUARY 25

Time	Event
8:00AM-9:00AM	**BREAKFAST**
9:00AM-10:30AM	**SCIENTIFIC SESSION X** Pediatric Cancers
10:30AM-10:50AM	**BREAK & EXHIBITS**
10:50AM-12:30PM	**SCIENTIFIC SESSION XI** A Look to the Future: Xenotransplantation
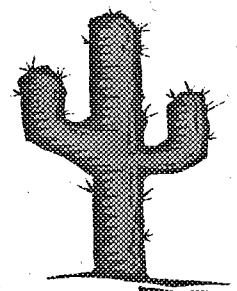
Saguaro
(Sah-war-oh)

**Large spiny cactus with arms
that never fit in your photo...**
Source: Sun Country Tours

Average Temperature in Scottsdale
& The Valley of the Sun in February

Max: 71° F. Min: 38° F.

Questions about Sponsorship

Corporations and others interested in a meeting sponsorship opportunity should contact:

Susan A. Ladwig, MA
Associate Director of Development
IBMTR/ABMTR Statistical Center
c/o Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee, WI, 53226, USA
414-456-8363
fax: 414-266-8471
email: susanl@hp04.biostat.mcw.edu
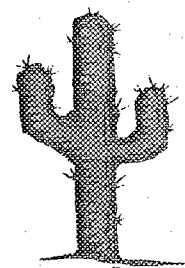
IBM**T**R
ABMTR

1998 Participants' Meeting

Keystone Resort, Colorado
January 8 – 14, 1998

MEDICAL
COLLEGE
OF WISCONSIN
CME
program

25 Years of International Scientific Collaboration continue...

From the Scientific Director - Mary M. Horowitz, MD, MS:

Dear Colleague:

IBMTR/ABMTR members can be proud of many accomplishments during the 25 years since its establishment by a small group of transplant pioneers. The IBMTR/ABMTR continues to play an important role in the global community of blood and marrow transplant research. Allogeneic and autologous blood and marrow transplant data are contributed to the Statistical Center by more than 400 participating centers, worldwide. Investigators from over 30 countries participate in studies using these data to address key issues in transplantation and cancer treatment. The IBMTR/ABMTR research program depends on these important contributions of time, effort and expertise.

A spirit of international scientific collaboration is the hallmark of our research effort and allows the Registries to be a vital resource for scientists, clinicians, patients and others involved in treatment of cancer and other life-threatening illnesses.

We hope to have each contributing team represented at the joint IBMTR/ABMTR Annual Participants' Meeting at Keystone Resort in 1998. We enthusiastically welcome attendance by senior and junior faculty members, clinical research associates and data managers, nursing staff and other allied health professionals. Team members' active participation in specific areas of interest and expertise add greatly to the overall program. Participants will play an active role in planning the Registries' scientific agenda. Non-members are also welcome to take advantage of this opportunity to learn about Registry activities and participate in the scientific program.

We look forward to seeing you in Keystone.

— *Mary Horowitz*

1998 Participants' Meeting
Keystone Resort — January 8-14, 1998

For Meeting Information call: 414-456-8377 or fax: 414-456-6530 For Housing call Keystone: 800-258-0437

Why you should attend the 1998 Participants' Meeting

Meeting Objectives

- to report on the "state of the art" in blood and marrow transplantation;
- to review Registry accomplishments;
- to discuss the progress of current and ongoing scientific studies;
- to set the Registries' scientific agenda for the next year;
- to provide training in data management and analysis for data managers, nurses and other allied health professionals working in blood and marrow transplantation.

Working Committee Meetings

IBMTR and ABMTR disease- and treatment-specific Working Committees are open to all interested in taking an ACTIVE role in ongoing and future studies. All Working Committee members should plan to attend.

Working Committees will review the past year's accomplishments, discuss current studies and plan future studies. Priorities for proposed studies will be established. Participation in these meetings is an opportunity to help determine the Registries' scientific agenda.

1998 IBMTR & ABMTR Working Committees

IBMTR/ABMTR Acute Leukemia	chairs:	Daniel Weisdorf –IBMTR
		Armand Keating –ABMTR
ABMTR Breast Cancer	chair:	Karen Antman
IBMTR/ABMTR CLL	chairs:	Emilio Montserrat –IBMTR
(Chronic Lymphocytic Leukemia)		Richard Champlin –ABMTR
IBMTR Chronic Myelogenous Leukemia	chair:	Phil McGlave
IBMTR GVH/GVL and Immune	chairs:	A John Barrett
Reconstitution		Olle Ringdén
IBMTR Histocompatibility,	chair:	Richard Champlin
Alternative Donors & Stem Cell Sources		
IBMTR Immune Deficiencies	chair:	Alexandra Filipovich
& Metabolic Diseases		
IBMTR Late Effects	chair:	Gérard Socié
IBMTR/ABMTR Lymphoma	chairs:	Koen Van Besien –IBMTR
		Hillard Lazarus, Julie Vose –ABMTR
ABMTR Multiple Myeloma	chair:	Sundar Jagannath
IBMTR/ABMTR Pediatric Cancer	chair:	Bruce Camitta
IBMTR Severe Aplastic Anemia	chair:	Jill Hows
IBMTR/ABMTR Solid Tumors	chair:	Patrick Stiff

Registration Information

Complete the enclosed Registration Form, including your VISA or MasterCard number, and fax to the Statistical Center at 414-456-6530. Checks, made payable to "The Medical College of Wisconsin - IBMTR", may be mailed to the Statistical Center. We regret that we cannot accept American Express for meeting registration fees. International funds must be submitted in US Dollars. All credit cards are processed in US Dollars and are subject to current exchange rates.

Registration Forms received prior to November 1 qualify for a preregistration discount. Those received on or after December 1 must pay the full conference rate, as indicated. Payment is due with the Registration Form.

Registration fees include admission to all sessions and exhibits, all IBMTR/ABMTR conference materials, abstract book and program, breakfast, coffee breaks and refreshments, and evening poster session receptions. Confirmation for each registered participant will be returned by fax.

1997 IBMTR/ABMTR MEETING REGISTRATION FEES

	before Nov 1	before Dec 1	on or after Dec 1
PARTICIPATING TEAM MEMBERS			
◆ MD/PhD	$395	$475	$550
◆ Allied Health Professionals*	$100	$125	$145
◆ Accompanying Persons	$150	$200	$250
CORPORATE MEMBERS	$400	$500	$600
NON-MEMBERS	$575	$675	$775

*Data Management Grants: A limited number of $500 grants are available on a first-come, first-serve basis to data management personnel attending the Data Management Workshops. To be eligible, data managers must be from centers currently reporting, or planning to report, autotransplants for breast cancer. The enclosed application must be returned to the Statistical Center prior to November 1, 1997 for consideration. See application for additional details. For more information contact D'Etta Waldoch Severson, CMP, Associate Director-International Programs at the Statistical Center at: 414-456-8377.

Conference Registration Cancellation: Meeting registration is fully refundable until November 30. All cancellations must be made in writing and may be faxed to the Statistical Center at 414-456-6530. Cancellations made on or after December 1 will be assessed a non-refundable handling fee of US $50; On January 1 the cancellation fee will increase to US $75. "No shows" without written notification will be assessed the full prepaid registration fee with no refund provision.

**1998 Participants' Meeting
Keystone Resort — January 8-14**

For Meeting Information call: 414-456-8377 or fax: 414-456-6530 For Housing call Keystone: 800-258-0437

Housing & Accommodations

Call or Fax Today for Reservations   Housing Form Due: December 1

A limited number of guest rooms and condominiums at special conference rates are reserved for IBMTR/ABMTR Meeting participants. The rates are available for 3 days before and after the conference for those wishing to extend their stay in Colorado's picturesque Arapahoe region. Take advantage of these special room rates, which represent substantial discounts during peak season for Keystone-area resorts.

Please complete the enclosed Housing Form and return it directly to Keystone Resort prior to December 1, 1997. It is strongly recommended that reservations be made early, as accommodations will be difficult and more costly to obtain after the deadline. Please indicate a major credit card number for the first and last night's deposit and applicable taxes. Reservations will not be held without a deposit. Reservations made after the deadline may not be available at the discounted conference rate and last minute requests may be impossible to accommodate (see Housing Form for more information).

1998 KEYSTONE RESORT ROOM RATES — Subject to Availability

Keystone Lodge:	$162/night single occupancy	$177/night double
Inn at Keystone:	$126/night single occupancy	$141/night double
Village Studio:	$163/night single or double	
Village 1 Bedroom:	$178/night single or double	
Village 2 Bedroom:	$262/single, double, triple or quad	
Resort Studio:	$146/night single or double	
Resort 1 Bedroom:	$168/night single or double	
Mountain Studio:	$183/night single or double	

Hotel Cancellation: Call Keystone Resort directly to cancel housing reservations. No shows, late arrivals and early departures will be charged the full room rate for the entire reserved period. THE IBMTR/ABMTR WILL NOT BE HELD RESPONSIBLE FOR INDIVIDUAL HOUSING CANCELLATIONS OR "NO SHOWS". HOUSING IS THE INDIVIDUAL RESPONSIBILITY OF EACH MEETING PARTICIPANT.

For Meeting Information call: 414-456-8377 or fax: 414-456-6530   For Housing call Keystone: 800-258-0437

Data Management Workshops

Featuring 2 Learning Tracks...   Friday, January 9, 1998

Due to enthusiastic feedback from participating IBMTR and ABMTR data management professionals, we are pleased to offer a full day of Data Management Workshops at the 1998 Participants' Meeting. Data managers, clinical research associates and research nurses will find topics of interest and opportunities for direct communication with on-site Statistical Center staff members leading informal, participatory Workshops on two tracks. Both tracks will discuss recent changes in IBMTR/ABMTR Registration and Reporting procedures.

> TRACK I   fundamental concepts for those attending the Workshops for the first time.
>
> TRACK II   designed for experienced data management and nursing professionals;
>   features special topics related to clinical research and audit management.

Additionally, StemCell Technologies Inc will demonstrate StemSoft software and their interrelated statistical analysis package. "Hands-on" training is available for those who preregister with StemCell Technologies Inc (details below). Data management personnel are invited to stay for the entire meeting.

$500 Grants for Data Management Workshops

The Statistical Center was awarded a grant from the US Department of Defense which will provide 30 data managers with $500 each to offset some of the travel costs associated with attending the Workshops. To be eligible, data managers must be from centers currently reporting, or planning to report autotransplants for breast cancer.

Grants are awarded as they are received, with priority given to first-time attendees. Please complete the enclosed Grant Application Form and return it by fax with your completed Registration Form as soon as possible. The deadline for Grant Application submission is November 1, 1997.

Grant awards go fast — do not delay!

StemCell Technologies Inc

StemCell Technologies Inc will offer full-day hands-on training sessions for their StemSoft line of products on Saturday - January 10, Sunday - January 11 and Monday - January 12. Training sessions will be limited to 20 participants each, on a first-come, first-serve basis, and are subject to cancellation if less than half full.

Data Managers and all 'end-users' of StemSoft software who want to achieve greater levels of performance and effectiveness with the software will benefit. The fee for participating in each session is $400. Please contact Ellen Low at StemCell Technologies Inc in Vancouver, British Columbia (Canada) at 800-667-0322 or 604-877-0713, or stemsoft@stemcell.com.

For Meeting Information call: 414-456-8377 or fax: 414-456-6530   For Housing call Keystone: 800-258-0437

More about Data Management

General Sessions

Introduction — **Barbara McGary, Manager of Information Systems, IBMTR/ABMTR**
Discuss Workshop format and dispell myths.

Scoring Common Toxicities — **Phil Rowlings, MD, Assistant Scientific Director, IBMTR/ABMTR**
Useful information for scoring common toxicities (GVHD, VOD) on IBMTR/ABMTR Report Forms.

Overview of Statistics — **Judith Veum Stone, Biostatistician, IBMTR/ABMTR**
What does the Statistical Center do with all those data? Discussion of outcome variables, in's and out's of working with the databases and basics of statistical analyses.

High-Dose Therapies — **Kathleen Kovatovic, RPh - Clinical Oncology & BMT Pharmacist**
Froedtert Memorial Lutheran Hospital, Milwaukee
How high-dose drug therapy in BMT differs from other disciplines.

Update on StemSoft — **David Reeves - Sr Programmer/Analyst, StemCell Technologies Inc., Vancouver, BC**
Quick demonstration on newest products available from StemCell Technologies. Opportunity to ask questions and sign up for full-day training seminars (see page 6 for details).

Two Learning Tracks...

TRACK I: First Timers

Registration & Reporting: Why Both? — **Barbara McGary, Manager of Information Systems, IBMTR/ABMTR**
Valuable information for first-timers regarding IBMTR/ABMTR registration and reporting procedures, why it is necessary to complete both registration and reporting forms and stay up-to-date.

Hands-on Registration 101 — **Sharon Nell, Communications Coordinator, IBMTR/ABMTR**
How to complete IBMTR/ABMTR *Registration* Forms from A-Z; helpful for those just getting started, or with questions on Registration procedures; question & answer session will follow.

Hands-on Reporting 101 — **Diane Knutson, Systems Coordinator, IBMTR/ABMTR**
Completing IBMTR/ABMTR *Reporting* Forms is not as difficult as it may first appear; obtain useful information to get started; opportunity to address specific questions on Reporting procedures.

TRACK II: For those who have attended IBMTR/ABMTR Workshops previously

Practical Aspects of Reporting: An Update — **Diane Knutson, Systems Coordinator, IBMTR/ABMTR**
For those who have heard Diane present "Hands-on Reporting 101", an update on working with IBMTR/ABMTR *Reporting* Forms, practical tips and suggestions for time-saving measures.

Registry Audit Survival Tactics — **Claudia Kabler-Babbitt, BSA, CCRC - Sr. Clinical Studies Coordinator**
Bone Marrow Transplant Program, Medical College of Wisconsin, Milwaukee
Ever wonder what an IBMTR/ABMTR Audit is like? Take it from Claudia! Practical tips for gathering data on a daily basis that will make audit day run like clockwork and sigh a gigantic breath of relief!

For Meeting Information call: 414-456-8377 or fax: 414-456-6530   For Housing call Keystone: 800-258-0437

Poster Sessions Combined with Evening Receptions

The late afternoon poster session on Monday, January 12 will be combined with a hosted reception featuring Keystone Resort's award-winning light buffet-style cuisine and beverages.

A $500 investigator award will be given for the best abstract submitted, as determined by IBMTR/ABMTR Committee Chairs.

Abstract Instructions Submission Deadline: November 15, 1997

1. Abstract must be typed on the enclosed ABSTRACT FORM.

2. CAPITALIZE entire title and UNDERSCORE author's names (underscoring or capitalizing for emphasis in text is unacceptable. Single space all typing (no space between title and body or between paragraphs). Indent each paragraph three spaces. Do not indent title. Draw special symbols in black ink.

3. Please do not reduce the abstract on a photocopy machine! Type abstract in 12 point type or larger. Abstracts submitted in a reduced format may not be included in the Abstract Book. Abstracts must be received by November 15, 1997 to ensure publication in the Abstract Book. ABSTRACT WILL APPEAR EXACTLY AS SUBMITTED. Smudges, errors, misspellings, faint type, etc. should be avoided.

4. Make the TITLE brief, clearly indicating the nature of the investigation. After the title, list the authors' names and institutional affiliations. Omit degrees, titles, institutional appointments, street addresses and zip or postal code.

5. Organize the body of the abstract as follows:

    *   A statement of the purpose of the study (preferably one sentence)
    *   A statement of the methods used
    *   A summary of the results presented in sufficient detail to support the conclusions
    *   A statement of conclusions reached. It is not satisfactory to state, "The results will be discussed" or "Other data will be presented.

6. Simple tables or graphs, neat and in black ink, may be included if they fit within the Abstract Form.

7. Abbreviations must be defined by placing them in parentheses after the full word the first time they appear. Use numerals to indicate numbers except when beginning sentences.

8. The material must be in camera-ready form, i.e., type must be laser quality, 300 dpi or better (no dot matrix). USE BLACK INK. Practice fitting text into the Abstract Form.

9. NO abstract may be presented if previously presented orally at a national or international meeting.

10. Submit abstract (original plus 2 copies) BEFORE NOVEMBER 15, 1997.

For Meeting Information call: 414-456-8377 or fax: 414-456-6530 For Housing call Keystone: 800-258-0437

Continuing Medical Education

The Medical College of Wisconsin (MCW) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians. MCW designates this continuing medical education (CME) activity for 23.5 credit hours in Category I of the Physician's Recognition Award of the American Medical Association. Each physician should claim only those hours of credit that he/she actually spent in the educational activity. MCW also designates this activity for 23.5 contact hours of continuing education for allied health professionals. Participants requesting credit should check the appropriate box on the enclosed Registration Form and must include social security number. A separate form will be available at the conference to designate actual hours attended which will be required for credit to be administered.

Disclosure

The Statistical Center of the IBMTR/ABMTR is committed to providing unbiased, balanced and objective educational and scientific programs. In accordance with ACCME guidelines, all 1998 Annual Meeting speakers are asked to provide relevant disclosure statements. Disclosures are on file at the Medical College of Wisconsin Continuing Medical Education office and will be available on-site at the Registration Desk for review.

Travel Assistance

CAUTION: Weather at the Denver airport is not a good indication of driving conditions in the mountains. Before heading west on I-70, check the local forecast and road conditions. Those not familiar with driving in winter conditions should consider using Resort Express shuttle service.

Hertz - the official car rental company

Hertz has been appointed the official car rental company for the 1998 IBMTR/ABMTR Participants' Meeting in Keystone. Special discount rates, with free unlimited mileage are guaranteed one week before and one week after the IBMTR/ABMTR meeting dates, subject to car availability. At the time of reservation booking, these rates will automatically be compared to Hertz published rates, assuring meeting participants are quoted the best comparable rates available at Denver International Airport. Standard rental conditions and qualifications apply, including minimum rental age. Check with your Hertz representative for further details.

> For reservations, call Hertz at 1-800-654-2240 in the US, in Canada at 1-800-263-0600, or check with your travel agent. Refer to CV# 42539.

Resort Express

Regularly scheduled shuttle service will meet you at the baggage claim level (level 5) at the Denver International Airport and deliver you to Keystone Lodge, with 16 daily departures. Mention the IBMTR/ABMTR Meeting at Keystone for discounted group fares: $70 per person round trip; $35 per person one way; $285 for 10 passenger vans one way; $395 for 6 passenger limosine one way.

> For reservations, call Resort Express at 800-334-7433 or 970-468-7600

For Meeting Information call: 414-456-8377 or fax: 414-456-6530   For Housing call Keystone: 800-258-0437

Questions About the Conference, Support/Exhibit Opportunities

For general questions about the Annual Participants'
Meeting please contact:

D'Etta Waldoch Severson, CMP
Associate Director-International Programs
IBMTR/ABMTR Statistical Center
414-456-8377
fax: 414-456-6530

Corporations and others interested in meeting
support and exhibit opportunities may contact:

Susan V. Ladwig, MA
Associate Director of Development
IBMTR/ABMTR Statistical Center
c/o Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee, WI, 53226, USA
414-456-8325
fax: 414-456-6530

MEDICAL COLLEGE OF WISCONSIN

CME *program*

1998 Participants' Meeting
January 8-14
Keystone Resort, Colorado, USA

For Meeting Information call: 414-456-8377 or fax: 414-456-6530 For Housing call Keystone: 800-258-0437

1998 IBMTR/ABMTR Participants' Meeting

Keystone Resort, Colorado
January 8 - 14, 1998

High Altitude Warning:

Keystone Resort is located 9,300 feet above sea level. If you have any health problems which may be complicated by high altitude, please consult with your physician before registering for the IBMTR/ABMTR Meeting.

NOTES:

1998 IBMTR/ABMTR Participants' Meeting

Keystone Resort, Colorado

January 8 - 14, 1998

High-Dose Chemotherapy With Autologous Hematopoietic Stem-Cell Support for Breast Cancer in North America

By Karen H. Antman, Philip A. Rowlings, William P. Vaughan, Corey J. Pelz, Joseph W. Fay, Karen K. Fields, Cesar O. Freytes, Robert Peter Gale, Bruce E. Hillner, H. Kent Holland, M. John Kennedy, John P. Klein, Hillard M. Lazarus, Philip L. McCarthy, Jr, Ruben Saez, Gary Spitzer, Edward A. Stadtmauer, Stephanie F. Williams, Steven Wolff, Kathleen A. Sobocinski, James O. Armitage, and Mary M. Horowitz

Purpose: To identify trends in high-dose therapy with autologous hematopoietic stem-cell support (autotransplants) for breast cancer (1989 to 1995).

Patients and Methods: Analysis of patients who received autotransplants and were reported to the Autologous Blood and Marrow Transplant Registry. Between January 1, 1989 and June 30, 1995, 19,291 autotransplants were reviewed; 5,886 were for breast cancer. Main outcomes were progression-free survival (PFS) and survival.

Results: Between 1989 and 1995, autotransplants for breast cancer increased sixfold. After 1992, breast cancer was the most common indication for autotransplant. Significant trends included increasing use for locally advanced rather than metastatic disease (*P* < .00001) and use of blood-derived rather than marrow-derived stem cells (*P* < .00001). One–hundred-day mortality decreased from 22% to 5% (*P* < .0001). Three-year PFS probabilities were 65% (95% confidence intervals [CIs], 59 to 71) for stage 2 disease, and 60% (95% CI, 53 to 67) for stage 3 disease. In metastatic breast cancer, 3-year probabilities of PFS were 7% (95% CI, 4 to 10) for women with no response to conventional dose chemotherapy; 13% (95% CI, 9 to 17) for those with partial response; and 32% (95% CI, 27 to 37) for those with complete response. Eleven percent of women with stage 2/3 disease and less than 1% of those with stage 4 disease participated in national cooperative group randomized trials.

Conclusion: Autotransplants increasingly are used to treat breast cancer. One–hundred-day mortality has decreased substantially. Three-year survival is better in women with earlier stage disease and in those who respond to pretransplant chemotherapy.

J Clin Oncol 15:1870-1879. © *1997 by American Society of Clinical Oncology.*

BREAST CANCER is the most common cancer and the second most common cause of cancer deaths in American women.[1] Survival of women with breast cancer correlates with extent of disease. Ten-year survival is 65% to 80% for women with disease confined to the breast.[2-4] Ten-year survival is 35% to 65% for those with one to three involved axillary lymph nodes, 30% to 40% for those with four to nine involved axillary nodes, and 15% to 30% in those with more than nine involved axillary nodes.[5-7] Recurrent disease tends to develop earlier in patients with multiple involved nodes and relapse risk persists for at least 20 years after mastectomy. Women with metastatic breast cancer have a median survival rate of approximately 2 years and a 2% to 5% probability of 5-year disease-free survival.[8-11]

Intensive therapy (high-dose chemotherapy with or without radiation therapy) with autologous hematopoietic stem-cell support (autotransplant) is increasingly used to treat breast cancer in women at high risk of persistent or recurrent disease. However, most reports of autotransplants include relatively few subjects and there are likely to be substantial reporting biases. One small randomized study of women with metastatic breast cancer shows a statistically significant advantage in both survival and disease-free survival for high-dose chemotherapy with bone marrow transplant versus conventional-dose chemotherapy.[12] Here we report results of autotransplants in more than 5,800 consecutive women receiving autotransplants at over 130 centers between 1989 and 1995.

METHODS

Patients

The Autologous Blood and Marrow Transplant Registry of North America (ABMTR) is a voluntary organization of more than 170 transplant institutions in the United States, Canada, and Central and South America that report data on consecutive autotransplants to a Statistical Center at the Medical College of Wisconsin. An autotransplant is defined as treatment with a sufficiently high dose of chemotherapy to require autologous bone marrow or blood-derived hematopoietic stem-cell support. The Statistical Center also collects data for allogeneic blood and bone marrow transplants (allotransplants) from centers that participate in the International Bone Marrow Transplant Registry, a similar but independent organization of allotransplant centers worldwide.

The ABMTR began data collection in 1992. Data were collected retrospectively for patients who received autotransplants between 1989 and 1992 and prospectively thereafter. Participating centers register basic information on consecutive autotransplants for all disease indications. Based on data collected in the Centers for Disease Control Hospital Surveys,[13,14] approximately half of North American autotransplants for all diseases were registered with the ABMTR during the study period. A list of participating centers is shown in the Appendix. Registration data from consecutive women with breast cancer who received an autotransplant at ABMTR centers between January 1, 1989 and June 30, 1995 were the subject of this analysis.

Data regarding disease type, age, sex, and posttransplant survival

were requested for all patients. Questions regarding pretransplant disease stage and chemotherapy responsiveness, date of diagnosis, graft type (bone marrow and/or blood-derived stem cells), high-dose conditioning regimen, and posttransplant disease progression were added to registration forms more recently. Although an attempt was made to collect this information for previously registered patients, these data are not available for all patients. Patients with primary (stages 2, 3, and inflammatory) and metastatic breast cancer were considered separately in the analysis. The ABMTR requests data on progression or death in registered patients at 6-month intervals.

Statistical Methods

Comparisons of patient and treatment characteristics over time used χ^2 test for categorical and Kruskal-Wallis test for continuous variables.[15] Probabilities of 100-day mortality (death in the first 100 days as a result of toxicity, disease progression, or both), progression-free survival (PFS), and overall survival were calculated using the Kaplan-Meier product limit estimate.[16] The log-rank test was used for comparisons of 100-day mortality, PFS, and survival between groups.[17]

RESULTS

Between January 1, 1989 and June 30, 1995, 19,291 patients receiving high-dose therapy with autologous hematopoietic stem-cell support were registered with the ABMTR. Of these, 5,886 (31%) had breast cancer. Between 1989 and 1995, autotransplants for breast cancer increased from 16% to 40% ($P < .00001$) of all autotransplants registered (Fig 1, Table 1). Numbers of autotransplants for breast cancer exceeded those for Hodgkin disease and non-Hodgkin lymphoma after 1992. By 1993 to 1994, breast cancer was the most common indication for stem-cell transplants of all types (Fig 1).

Numbers of patients reported per year, age at transplant, pretransplant disease stage, source of stem cells, and 100-day mortality are listed in Table 1. The distribution of disease stage at transplantation changed from 7% local and 93% metastatic disease in 1989 to approxi-
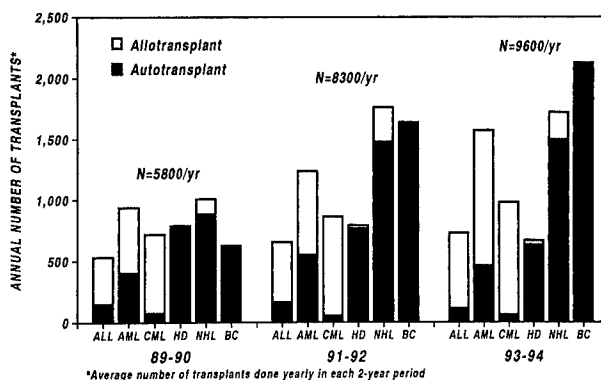
Fig 1. Numbers of allotransplants (hematopoietic stem cells collected from a donor) and autotransplants by year by disease for most common indications.

Table 1. Autotransplants for Breast Cancer Registered With the ABMTR

	1989	1990	1991	1992	1993	1994	January to June 1995	P
No. of patients	272	342	683	1,069	1,189	1,513	818	
Percent of all autotransplants registered	16	16	25	33	33	39	40	< .00001
Autotransplants for breast cancer								
No. of centers reporting	34	45	66	85	99	105	101	
Median transplants per center	3	5	6	7	6	8	5	.005
Range	1-58	1-44	1-44	1-71	1-59	1-86	1-63	
Stage immediately before high-dose chemotherapy and autotransplant								
No. assessable*	213	313	650	1,005	1,088	1,404	721	< .00001
Local disease† (%)	7	16	23	34	31	39	49	
Metastatic (%)	93	83	77	65	68	60	50	
Other‡ (%)	< 1	1	< 1	1	1	1	1	
Age, years								
No. assessable	272	341	678	1,059	1,123	1,461	817	< .00001
Median	41	42	44	44	45	45	45	
Range	23-64	24-66	22-72	25-65	24-66	22-69	22-71	
Interval diagnosis to transplant (years)								
No. assessable	237	299	614	960	1,106	1,392	774	< .00001
< 1 (%)	18	24	31	44	42	49	57	
1-2 (%)	28	19	16	14	12	13	10	
> 2 (%)	54	57	53	42	46	38	33	
Graft type								
No. assessable	162	215	474	813	1,189	1,447	760	< .00001
BM (%)	81	79	58	42	30	19	10	
BM + PBSC (%)	5	7	22	33	30	25	18	
PBSC (%)	14	14	20	25	40	56	72	
Conditioning regimen								
No. assessable	140	183	423	735	870	1,174	587	< .00001
CBP (%)	7	4	11	13	9	14·	6	
CT (%)	25	22	23	23	21	21	21	
CTCb (%)	18	16	15	28	37	39	44	
CTM (%)	6	2	6	4	4	2	1	
ICE (%)	3	10	8	7	6	4	4	
CTHu (%)	8	4	5	4	3	3	4	
CEP (%)	3	3	5	3	2	1	2	
Other (%)	30	37	27	18	18	16	18	
100-day mortality								
No. assessable	265	340	679	1,034	1,153	1,366	784	< .00001
%	22	15	11	6	6	4	5	

Abbreviations: BM, bone marrow; PBSC, peripheral-blood stem cells; C, cyclophosphamide; B, carmustine; P, cisplatin; T, thiotepa; Cb, carboplatin; M, mitoxantrone; I, ifosfamide; E, etoposide; Hu, hydroxyurea.

*Information for all variables not available for all patients; registration forms were revised in 1992 and 1993 to capture additional information.

†Local disease = stage 2, 3; and inflammatory breast cancer.

‡Patients with locally persistent or recurrent disease post–conventional therapy.

mately 50% local and 50% metastatic disease in 1995 (P < .00001). This is reflected in the interval from diagnosis to transplant, which decreased over the study period. By 1995, 57% of transplants for breast cancer were performed within 1 year of diagnosis.

Use of blood-derived cells alone or in combination with bone marrow increased from 19% to 90% (P < .00001) in these 6 years. Various preparatory regimens were used, with only the combination of cyclophosphamide, thiotepa, and carboplatin (CTCb) used in more than 25% of all

patients. An important finding was decreasing 100-day mortality, from 22% in 1989 to 5% in 1995 (P < .00001).

High-Risk Primary Breast Cancer

Characteristics of women who received autotransplants for stage 2, 3, and inflammatory breast cancer are listed in Table 2. Eleven percent were treated as part of randomized cooperative group trials. Although most patients had stage 2 or 3 breast cancer and ≥ 10 involved axillary nodes, some transplants were performed for inflammatory

Table 2. Autotransplants for Stage 2, 3, or Inflammatory Breast Cancer

	No. assessable*	No.	%
No. registered	1,747		—
Median age, years	1,731	44	
Range		22-69	
Stage pretransplant			
2	1,613†	750	46
3		603	37
Inflammatory		260	17
Months from diagnosis to transplant	1,636	7	
Range		2-16	
No. of nodes positive	542		
< 10		150	28
≥ 10		392	72
ER positive	479	298	62
Principal adjuvant chemotherapy			
CAF	491	314	64
Graft type	1,527		
BM		502	32
BM + PBSC		450	30
PBSC		555	38
High-dose chemotherapy regimen used	1,370		
CT		432	32
CTCb		403	29
CBP		220	16
CTM		52	4
ICE		78	6
CEP		26	2
Other		156	11
100-day mortality (%)	1,668		3

Abbreviations: ER, estrogen receptor; C, cyclophosphamide; A, doxorubicin; F, fluorouracil; BM, bone marrow; PBSC, peripheral-blood stem cells; B, carmustine; P, cisplatin; T, thiotepa; Cb, carboplatin; M, mitoxantrone; E, etoposide; Hu, hydroxyurea.

*Information for all variables not available for all patients. Registration forms were revised in 1992 and 1993 to capture additional information.

†One hundred thirty-four additional patients stage 2 v 3 v inflammatory not specified.

breast cancer (17%) or for women with less than 10 involved axillary nodes (28%). Kaplan-Meier estimates of survival and PFS by disease stage are shown in Fig 2; 3-year probabilities are listed in Table 3.

Metastatic Breast Cancer

Characteristics of women who received autotransplants for metastatic breast cancer are listed in Table 4. Fewer than 1% were treated on randomized cooperative group trials. Most patients had chemotherapy-sensitive disease (complete or partial response before transplant) and either visceral or bone disease. Median survival was 19 months (Fig 2). Three-year PFS and survival probabilities are listed in Table 3. Women with a complete response to chemotherapy pretransplant had higher survival and PFS than those with either a partial response or resistant disease (Fig 3).

Second Malignancies

Data regarding second malignancies were available for 2,045 women. There were 13 cancers reported: four myelodysplastic syndromes, two endometrial carcinomas, one ovarian carcinoma, one squamous cell carcinoma, one transitional cell carcinoma of the bladder, one Hurthle cell tumor of the thyroid, one lung carcinoma, one glioblastoma, and one cervical cancer.

DISCUSSION

These data indicate several interesting aspects of autotransplants for breast cancer. First, the annual frequency of autotransplants has increased substantially, from fewer than 300 reported to the ABMTR in 1989 to approximately 1,500 presently. Second, an increasing proportion are for women with locally advanced disease: less than 10% in 1989 versus approximately 50% presently. As a correlate, the interval from diagnosis to transplant has decreased substantially; less than 20% of transplants were performed within 1 year of diagnosis in 1989 versus more than 50% presently. A third trend is increasing use of blood-derived rather than bone marrow–derived grafts: 14% in 1989 versus more than 70% presently. Finally, 100-day mortality also decreased substantially, from more than 20% in 1989 versus 5% presently. This probably reflects several factors, including selection of patients with less advanced disease and better performance status.

Women with locally advanced (stage 2 and 3) breast cancer who receive autotransplants differ from the general population of women presenting with breast cancer. Median age was 44 years and more than 70% had more than nine involved lymph nodes. These data contrast with typical women with breast cancer, whose median age is approximately 60 years, of whom approximately 5% have more than nine involved lymph nodes.[6,7] These differences reflect the substantial selection factors for transplant and underscore the importance of comparing autotransplants and chemotherapy in comparable subjects. A Toronto study reported that 28% of patients referred for one randomized trial of high- versus lower-dose therapy were ineligible because of occult metastatic disease identified by the required pretransplant evaluation.[18] Thus, differences observed between patients who received autotransplants and those who received conventional-dose chemotherapy in historical data bases may result from selection of patients without occult metastases.

Women with metastatic (stage 4) disease who received autotransplants were also somewhat atypical. Median age was 44 years and 58% had cancers with estrogen receptors. Approximately 28% had a complete response to chemotherapy, but 24% had disease progression. These data contrast with typical women with stage 4 breast cancer

A

B
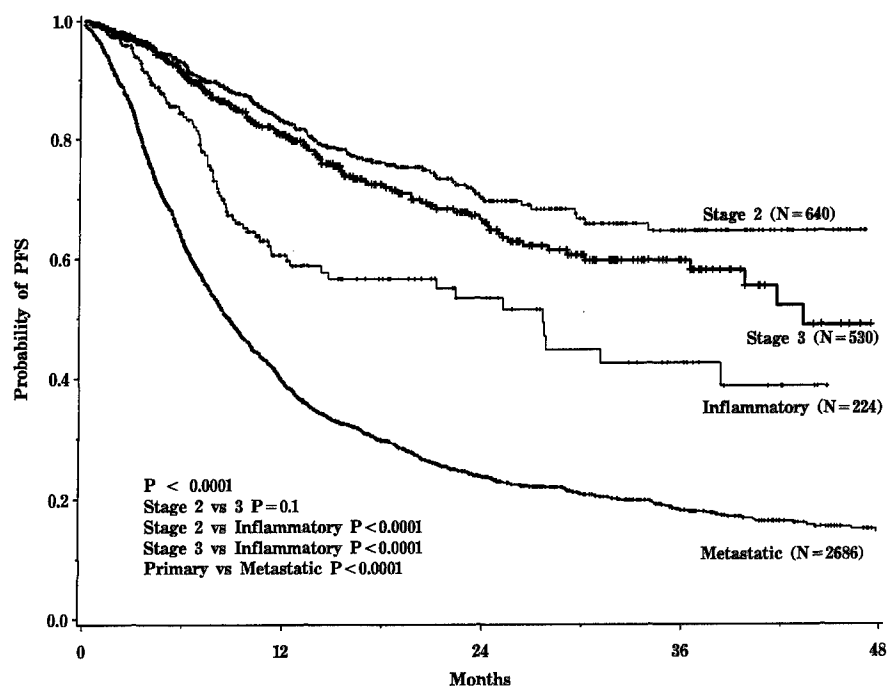
Fig 2. Kaplan-Meier estimates of PFS (A) and survival (B) after auto-transplants for primary (stage 2, 3, or inflammatory) and metastatic breast cancer.
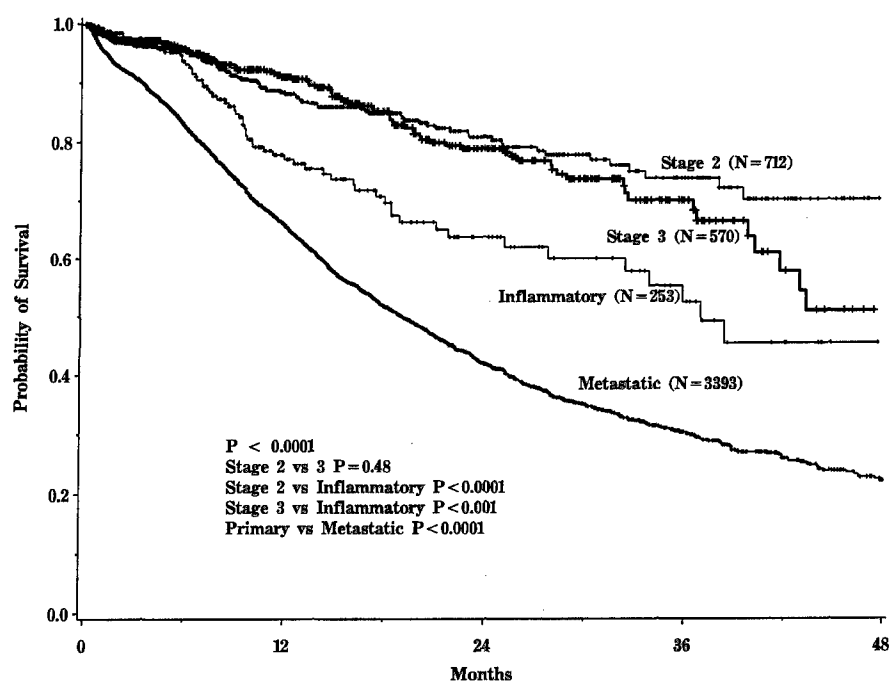
Table 3. Three-year Kaplan-Meier Estimates of PFS and Overall Survival After Autotransplants for Breast Cancer

Stage	PFS (%)	95% CI	Survival (%)	95% CI
2 (2 to 5 cm or involved lymph nodes)	65	59-71	74	68-80
3 (> 5 cm or fixed to the chest wall)	60	53-67	70	63-77
Inflammatory	42	31-53	52	40-64
Metastatic	18	16-20	30	28-32
Response to chemotherapy				
In complete remission	32	27-37	46	40-52
In partial remission	13	9-17	29	25-33
Not responding	7	4-10	16	12-20

whose median age is approximately 60 years, of whom 60% to 70% have cancers with estrogen receptors. These differences again underscore the importance of comparing autotransplants and chemotherapy in comparable subjects. Nevertheless, one small randomized study showed a statistically significant advantage in both survival and disease-free survival for high-dose chemotherapy with bone marrow transplant versus conventional-dose chemotherapy in women with metastatic disease.[12]

Results of autotransplants correlated with disease stage. Women with stage 2 or 3 disease had better PFS and survival than those with stage 4 disease. However, there was no difference in PFS or survival between women with stage 2 versus 3 disease. Among women with metastatic (stage 4) disease, those with a complete response to pretransplant chemotherapy fared better than those with a partial response. The latter fared better than those with stable disease or progression. Women with tumors unresponsive to lower-dose treatment are very unlikely to achieve long-term disease-free survival after autotransplant.

The correlation between stage and chemotherapy response and outcome is not surprising. Similar results are reported for conventional treatments. Better transplant outcome in "better" subjects does not mean that transplants should be performed earlier or indicate whether transplants are better than conventional therapy. These questions are best addressed in prospective studies, several of which are underway (Table 5). In this survey, only 11% of women with stage 2 or 3 disease and fewer than 1% of those with stage 4 disease participated in national cooperative group randomized trials. During the time covered by this survey, three cooperative group trials were open for enrollment in the United States, one for metastatic disease and two for adjuvant therapy. Additionally, randomized trials, including the one published study[12] and those listed in Table 5, are not designed to answer other important questions such as relative efficacy of various high-dose regimens, supportive care technologies, or even patient-, disease-, and treatment-related factors important

for transplant outcome. The ABMTR is an important resource for addressing such issues. Data collected by the Centers for Disease Control hospital survey[13,14] suggest that approximately half of all autotransplants in North America are reported to the ABMTR. We believe that reporting of autotransplants for breast cancer is similar, making available a substantial proportion of cases for study. Registry audits ensure that this sample is unselected and that data are accurate. Because participation in the ABMTR is voluntary, it is possible that participating centers differ from nonparticipating centers. For example, nonacademic centers may be less likely to participate than academic centers, although the ABMTR includes many

Table 4. Autotransplants for Metastatic Breast Cancer

	No. assessable*	No.	%
No. registered	3,451		
Median age, years	3,398	44	
Range		22-72	
Sensitivity to chemotherapy pretransplant	3,411		
Complete or partial response		2,134	63
Stable or progressive disease		595	17
Undetermined		682	20
Sites of metastatic disease	1,212		
Viscera (no CNS)†		593	49
Bone or bone marrow ± soft tissue‡		328	27
Soft tissue alone		273	23
CNS§		18	1
ER positive	1,203	700	58
Interval, diagnosis to transplant (years)	3,298		
< 1		687	21
1-2		568	17
> 2		2,038	62
Graft type	3,018		
BM		993	33
PBSC		1,373	46
BM + PBSC		652	21
Conditioning regimen	2,522		
CTCb		899	36
CT		416	17
ICE		132	5
CTHu		146	6
CTM		71	3
CBP		202	8
CEP		60	2
Other		596	23
100-day mortality (%)	3,395		10

Abbreviations: ER, estrogen receptor; BM, bone marrow; PBSC, peripheral-blood stem cells; C, cyclophosphamide; B, carmustine; P, cisplatin, T, thiotepa; Cb, carboplatin; M, mitoxantrone; E, etoposide; Hu, hydroxyurea.

*Information for all variables not available for all patients. Registration forms were revised in 1992 and 1993 to capture additional information.

†Includes patients with or without bone, bone marrow, or soft tissue involvement.

‡Excludes patients with visceral or CNS involvement.

§Includes patients with or without visceral, bone, bone marrow, or soft tissue involvement.

A

P < 0.0001
CR vs PR   P < 0.0001
PR vs Resistant   P < 0.0001

CR (N = 587)

PR (N = 943)

Resistant (N = 500)

B

P < 0.0001
CR vs PR   P < 0.0001
PR vs Resistant   P < 0.0001

CR (N = 680)

PR (N = 1145)

Resistant (N = 592)
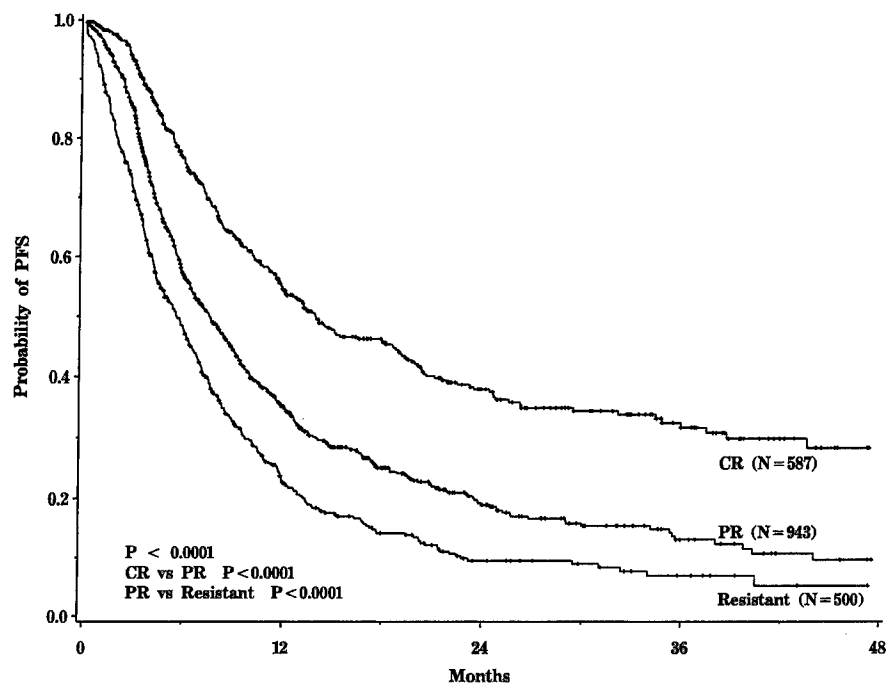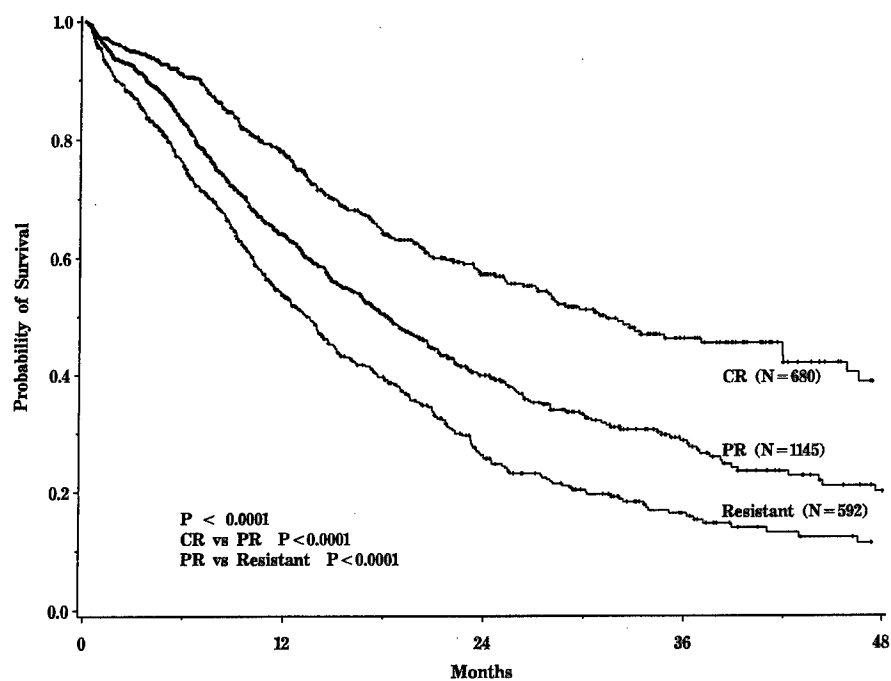
Fig 3. Kaplan-Meier estimates of PFS (A) and survival (B) after autotransplant for metastatic breast cancer by responsiveness to chemotherapy pretransplant. CR, complete response to conventional-dose chemotherapy pretransplant; PR, partial response; resistant, stable or progressive disease pretransplant.

Table 5. Ongoing Randomized Trials of Autotransplants in Breast Cancer by Stage

Eligible Stage	Study Sponsor	Standard Initial Therapy	High-dose Regimen	Control
Stage 2				
No. of involved lymph nodes				
≥ 4	Milan/Italy	None	HDS	E × 3, CMF × 6
≥ 4	Inter-Scandinavian	CEF × 4	CTCb	CEF × 4
≥ 4	Italian	CEF × 4	CEL	CEF × 2
≥ 4	Dutch	CEF × 4	CTCb	CEF × 1
4-9	Duke	AF	CBP	No more therapy v CBP alone
≥ 6	ICG (Manchester)	CE × 4	CTCb	CE × 4
≥ 8	SFGM/FNCCC	CEF × 4	CMitoxL	No further therapy
≥ 10 or > 4 high risk	IBCSG		CE × 3	AC or EC × 4, then CMF × 3
≥ 10	CALGB	CAF × 4	CBP	Conventional-dose CBP
≥ 10	German Multicenter	CE × 4	CTMitox	CMF × 3
≥ 10	ECOG	CAF × 4	CT	No further therapy
Stage 3				
	Milan/Italy	None	HDS	E × 3, then CMF × 6
	SFGM/FNCCC	Chemotherapy × 4	CMitoxL	Conventional chemotherapy
	IBCSG		CE × 3	AC or EC × 4, then CMF × 3
	CALGB	A × 4	CTCb	Continuous CMF × 16 weeks
	German Multicenter	CE × 4	CTMitox	CMF × 3
Stage 4				
	Duke (CRs only)	AFM × 4	CBP	CBP at relapse
	Duke (bone only)	AFM × 4, radiation	CBP	CBP at relapse
	Philadelphia Intergroup	CAF × 6	CTCb	CMF × 2 years
	SFGM/FNCCC	Chemotherapy × 4	CMitoxL	Conventional chemotherapy

Abbreviations: ICG, International Collaborative Group (Manchester); SFGM, Societe Francaise de Greffe du Muelle; FNLCC, Federation Nationale des Centres de Lutte Centra le Cancer; CALGB, Cancer and Leukemia Group B; ECOG, Eastern Cooperative Oncology Group; SWOG, Southwest Oncology Group; IBCSG, International Breast Cancer Study Group; C, cyclophosphamide; E, epirubicin; A, doxorubicin; F, fluorouracil; Cb, carboplatin; M, methotrexate; P, cisplatin; L, melphalan; Mitox, mitoxantrone; T, thiotepa; HDS, high-dose sequential therapy.

nonacademic centers. It is also possible that centers with poorer results do not report their data, although outcomes in our analyses are similar to those of large nonparticipating centers. Of interest, prior surveys of worldwide allogeneic transplant activity[19-21] suggest that centers in the IBMTR are similar to nonparticipating centers in characteristics and outcome. Finally, analyses of differences among centers are difficult for centers that perform fewer than 30 autotransplants. However, small centers, considered as a group, did not perform worse than large centers

in this study. The ABMTR provides an important observational data base that will complement data from randomized trials and with which one can monitor trends and assess new technology in blood and marrow transplantation. Registry data will be critical for extrapolating results of these trials, which tend to be applied in restricted populations, to other patients, and for evaluating the impact of preparative regimens, demographic factors, prior treatment, and other variables on transplant outcome.

APPENDIX
Institutions That Report Breast Cancer Cases to the ABMTR

Country/Institution	City	Country/Institution	City
Argentina		Baptist Regional Cancer Center	Jacksonville, FL
Alexander Fleming Institute	Buenos Aires	University of Kansas Medical Center	Kansas City, KS
Centro de Internacion e Investigation	Buenos Aires	Scripps Clinic & Research Foundation	La Jolla, CA
Hospital Privado de Oncologia	Buenos Aires	Dartmouth-Hitchcock Medical Center	Lebanon, NH
Navy Hospital "Pedro Mallo"	Buenos Aires	University of Kentucky Medical Center	Lexington, KY
Hospital Privado de Cordoba	Cordoba	University of Arkansas for Health	
Austria		Sciences	Little Rock, AR
Donauspital	Vienna	UCLA Center for Health Sciences	Los Angeles, CA
Brazil		USC/Norris Cancer Hospital	Los Angeles, CA
Hospital de Clinicas	Curitiba	James Graham Brown Cancer Center	Louisville, KY
Hospital Nossa Senhora das Gracas	Curitiba	University of Wisconsin	Madison, WI

Canada
    University of Calgary   Calgary
    Royal Victoria Hospital   Montreal
    Sacré Coeur Hospital   Montreal
    Northeastern Ontario Regional Cancer
      Centre   Sudbury
    Toronto Hospital   Toronto
    Vancouver General Hospital   Vancouver
    Manitoba Cancer Treatment Center   Winnipeg
Cuba
    Hermanos Ameijeiras Hospital   Havana
Mexico
    Institute Nacional de Cancerologia   Mexico City
    Centro de Hematologia y Medicina
      Interna   Puebla
Russia
    Petrov Research Institute of Oncology   St. Petersburg
United States
    Presbyterian Health Care Services   Albuquerque, NM
    University of Michigan Medical Center   Ann Arbor, MI
    Arlington Cancer Center   Arlington, TX
    Emory Clinic   Atlanta, GA
    Southwest Regional Cancer Center   Austin, TX
    Johns Hopkins Hospital   Baltimore, MD
    University of Maryland Cancer Center   Baltimore, MD
    Mary Bird Perkins Cancer Center   Baton Rouge, LA
    Alta Bates Hospital   Berkeley, CA
    University of Alabama at Birmingham   Birmingham, AL
    Dana-Farber Cancer Institute   Boston, MA
    Montefiore Medical Center   Bronx, NY
    Roswell Park Cancer Institute   Buffalo, NY
    University of North Carolina Chapel Hill   Chapel Hill, NC
    Medical University of South Carolina   Charleston, SC
    University of Virginia Medical Center   Charlottesville, VA
    Rush Presbyterian/St. Luke's Medical
      Center   Chicago, IL
    University of Chicago Medical Center   Chicago, IL
    Jewish Hospital of Cincinnati   Cincinnati, OH
    University Hospital Cincinnati   Cincinnati, OH
    Case Western Reserve University
      Hospital   Cleveland, OH
    Cleveland Clinic Foundation   Cleveland, OH
    University of South Carolina   Columbia, SC
    Ohio State University Hospital   Columbus, OH
    Baylor University Medical Center   Dallas, TX
    Miami Valley Hospital   Dayton, OH
    Presbyterian/St. Luke's Hospital   Denver, CO
    Wayne State University   Detroit, MI
    City of Hope National Medical Center   Duarte, CA
    University of Connecticut Health Center   Farmington, CT
    Bone Marrow & Stem Cell Institute of
      Florida   Fort Lauderdale, FL
    Harris Methodist Oncology Program   Fort Worth, TX
    University of Florida, Shands Hospital   Gainesville, FL
    East Carolina University School of
      Medicine   Greenville, NC
    Hackensack Medical Center   Hackensack, NJ
    Hinsdale Hematology-Oncology
      Associates   Hinsdale,
    Queen's Cancer Center   Honolulu, HI
    St. Francis Medical Center   Honolulu, HI
    Baylor College of Medicine   Houston, TX

M.D. Anderson Cancer Center   Houston, TX
Indiana University Hospital &
    Outpatient Center   Indianapolis, IN
Methodist Hospital of Indiana   Indianapolis, IN
St. Vincent Hospital & Health Care Ctr.   Indianapolis, IN
North Shore University Hospital   Manhasset, NY
Marshfield Clinic   Marshfield, WI
Loyola University Medical Center   Maywood, IL
Methodist Hospital Central   Memphis, TN
Baptist Hospital of Miami   Miami, FL
Froedtert Memorial Lutheran   Milwaukee, WI
St. Luke's Medical Center   Milwaukee, WI
Abbott Northwestern Hospital   Minneapolis, MN
University of Minnesota   Minneapolis, MN
West Virginia University   Morgantown, WV
Vanderbilt University Medical Center   Nashville, TN
Columbia Presbyterian Medical Center   New York, NY
Mount Sinai Medical Center   New York, NY
Medical Center of Delaware   Newark, DE
Hoag Cancer Center   Newport Beach, CA
University of Oklahoma Health
    Sciences Center   Oklahoma City, OK
University of Nebraska Medical Center   Omaha, NE
Saint Joseph Hospital   Orange, CA
Lutheran General Hospital   Park Ridge, IL
Hematology Associates   Peoria, IL
Hahnemann University Hospital   Philadelphia, PA
Temple University Comprehensive
    Cancer Center   Philadelphia, PA
University of Pennsylvania Hospital   Philadelphia, PA
Shadyside Hospital   Pittsburgh, PA
University of Pittsburgh   Pittsburgh, PA
Cancer Center of Boston   Plymouth, MA
North Shore Hem/Onc Assoc   East Setauket, NY
Oregon Health Sciences Univ.   Portland, OR
Roger Williams Medical Center   Providence, RI
Cancer & Blood Institute of the Desert   Rancho Mirage, CA
Washow Regional Cancer Center   Reno, NV
Mayo Clinic Rochester   Rochester, NY
University of Rochester   Rochester, NY
Sutter Memorial Hospital   Sacramento, CA
University of California Davis Cancer
    Center   Sacramento, CA
Latter Day Saints Hospital   Salt Lake City, UT
University of Utah Medical Center   Salt Lake City, UT
South Texas Cancer Institute   San Antonio, TX
University of Texas Health Sciences
    Center   San Antonio, TX
University of CA, San Diego   San Diego, CA
University of CA, San Francisco
    Medical Center   San Francisco, CA
Mayo Clinic Scottsdale   Scottsdale, AZ
LSU Medical Center-Shreveport   Shreveport, LA
Memorial Medical Center   Springfield, IL
Tufts University School of Medicine   Springfield, MA
Methodist Hospital/Nicollet Cancer
    Center   St. Louis Park, MN
St. Louis University Medical Center   St. Louis, MO
Bennett Cancer Center   Stanford, CT
Stanford University Hospital   Stanford, CA
SUNY-Health Science Center   Syracuse, NY

H. Lee Moffitt Cancer Center	Tampa, FL	Walter Reed Army Medical Center	Washington, DC
Arizona Cancer Center	Tucson, AZ	Westlake Comprehensive Cancer Center	Westlake Village, CA
St. Francis Hospital	Tulsa, OK	St. Francis Hospital	Wichita, KS
New York Medical College	Valhalla, NY	Wake Forest University	Winston-Salem, NC
George Washington University Medical		University of Massachusetts Medical	
Center	Washington, DC	Center	Worcester, MA

REFERENCES

1. Wingo P, Tong T, Bolden S: Cancer Statistics, 1995. CA Cancer J Clin 45:8-30, 1995

2. Fisher B, Bauer M, Margolese R, et al: Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. N Engl J Med 312:665-673, 1985

3. Fisher B, Redmond C, Poisson R, et al: Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med 320:822-828, 1989

4. Veronesi U, Saccozzi R, Del Vecchio M, et al: Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancer of the breast. N Engl J Med 305:6-11, 1981

5. Valagussa P, Bonadonna G, Veronesi U: Patterns of relapse and survival following radical mastectomy: Analysis of 716 consecutive patients. Cancer 41:1170-1178, 1978

6. Fisher E, Sass R, Fisher B: Pathologic findings from the national surgical adjuvant project for breast cancers (protocol no. 4). Cancer 53:712-723, 1984

7. Nemoto T, Vana J, Bedwani RN, et al: Management and survival of female breast cancer: Results of a national survey by the American College of Surgeons. Cancer 45:2917-2924, 1980

8. Clark G, Sledge GW, Osborne CK, et al: Survival from first recurrence: Relative importance of prognostic factors in 1,015 breast cancer patients. J Clin Oncol 5:55-61, 1987

9. Mick R, Begg CB, Antman K, et al: Diverse prognosis in metastatic breast cancer: Who should be offered alternative initial therapies? Breast Cancer Res Treat 13:33-38, 1989

10. Henderson IC: Chemotherapy for advanced disease, in Harris JR, Hellman S, Henderson IC, et al (eds): Breast Diseases. Philadelphia, PA, Lippincott, 1987, pp 428-479

11. Hortobagyi GN, Buzdar AU, Bodey GP, et al: High-dose induction chemotherapy of metastatic breast cancer in protected environment: A prospective randomized study. J Clin Oncol 5:178-184, 1987

12. Bezwoda WR, Seymour L, Dansey RD: High-dose chemotherapy with hematopoietic rescue as primary treatment for metastatic breast cancer: A randomized trial. J Clin Oncol 13:2483-2489, 1995

13. National Hospital Discharge Survey for 1990 and 1991. US Department of Health and Human Services, Public Health Service, Center for Disease Control. National Center for Health Statistics. Hospital Care Statistics Branch, Hyattsville, MD

14. Graves EJ: Detailed diagnoses and procedures, National Hospital Discharge Survey, 1989. Vital & Health Statistics-Series 13: Data From the National Health Survey. 108:1-236, 1991

15. Kruskal WH, Wallis WA: Use of ranks in one-criterion variance analysis. J Am Stat Assoc 47:583-621, 1952

16. Kaplan EL, Meier P: Nonparametric estimation from incomplete observations. J Am Stat Assoc 53:457-481, 1958

17. Cox DR: Regression models and life tables. J R Stat Soc B 34:187-202, 1972

18. Crump M, Prince M, Goss P: Outcome of extensive evaluation of women with > 10 positive axillary lymph nodes prior to adjuvant therapy for breast cancer. Anti Cancer Drugs 6:71, 1995 (abstr)

19. Bortin MM, Rimm AA: Increasing utilization of bone marrow transplantation. II. Results of 1985-1987 survey. Transplantation 48:453-458, 1989

20. Bortin MM, Horowitz MM, Rimm AA: Increasing utilization of allogeneic bone marrow transplantation. III. Results of the 1988-1990 survey. Ann Intern Med 116:505-512, 1992

21. Silberman G, Crosse MG, Peterson EA, et al: Availability and appropriateness of allogeneic bone marrow transplantation for chronic myeloid leukemia in 10 countries. N Engl J Med 331:1063-1067, 1994

Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation

Chien-Shing Chen, MD., Ph.D.,[1,2] Kristy Seidel, MS.,[1] James O. Armitage, MD., [3]

Joseph W. Fay , MD., [4] Frederick R. Appelbaum, MD., [1,2] Mary M. Horowitz, MD., MS., [5]

Elizabeth J. Shpall, MD., [6] Paul L. Weiden, MD., [7] Karen S. Antman, MD., [8]

Richard E. Champlin, MD., [9] John H. Kersey, MD., [10] and Keith M. Sullivan, MD. [1,2]

[1] Fred Hutchinson Cancer Research Center, and [2] University of Washington, Seattle, WA; [3] University of Nebraska Medical Center, Omaha, NE; [4] Baylor University Medical Center, Dallas, TX; [5] International Bone Marrow Transplant Registry, and Medical College of Wisconsin, Milwaukee, WI; [6] University of Colorado Health Science Center, Denver, CO; [7] Virginia Mason Clinic, Seattle, WA; [8] Columbia Presbyterian Medical Center, New York, NY; [9] M.D. Anderson Cancer Center and University of Texas, Houston, TX; and [10] University of Minnesota Cancer Center, Minneapolis, MN.

1

ABSTRACT

Background   Overdoses in high-dose chemotherapy before hematopoietic cell transplantation are serious events but their frequency and nature are unknown.

Methods The American Society for Blood and Marrow Transplantation (ASBMT) conducted an anonymous national survey to identify errors and safety practices for the administration of high-dose chemotherapy.

Results The questionnaire was returned from 115 (68%) of 170 hematopoietic transplant centers in the United States. Ninety-four (83%) were university or affiliated centers; 19 (17%) were community hospitals and 41 (36%) of the programs were founded since 1990. Characteristics of responding centers were compared with those of all centers reporting to transplant registry databases. There were more responses returned from larger centers (p=0.04). Fifteen (13%) of the 115 responding centers reported a total of 18 patients given inadvertent overdoses of cisplatin (n=3), carboplatin (n=2), busulfan (n=2), cytosine arabinoside (n=2), cyclophosphamide (n=2), interleukin-2 (n=2), or other agents (n=5) between 1989 and 1994. Cumulative drug doses given as a daily dose (six cases), and nursing infusion errors (six cases) were the most common errors. The estimated chemotherapy overdose error rate was 0.06%, or 6 cases/10,000 transplants, with 95% confidence limits of 0.03%-0.11%. The overdose rates among more experienced centers in operation before 1990 were lower than among newer centers (p<0.01). Large centers (>100 transplants performed in 1994) also had less frequent errors than medium-sized centers (21-100 transplants, p=0.03).

Conclusions Although rare in this self-reporting survey, overdoses were noted in centers, especially among recently established units. Current safety practices emphasize multidisciplinary checkpoints at the physician, pharmacist, nursing and institutional levels. Based on these survey results, recommendations for further safeguards for high-dose chemotherapy administration are proposed.   (267 words)

INTRODUCTION

High-dose chemotherapy followed by marrow or peripheral blood stem cell transplantation is widely employed for the treatment of hematologic and malignant disorders [1-3]. Recent episodes of accidental overdose of myeloablative chemotherapy have been widely publicized and call into question the safety of these procedures [4-6]. However, the frequency and nature of overdoses are poorly understood as are the implementation and reliability of practices designed to safeguard this therapy.

Errors in medical practice take many forms including mistakes in physician ordering of treatments, nursing or pharmacy administration of medications, surgical practice and blood transfusion [7-10]. The Harvard Medical Practice Study found that 3.7 % of hospitalized patients in New York state in 1984 suffered iatrogenic injuries, with negligent care responsible for 28% of these injuries [7]. Based on that study, it has been estimated that unintended injuries were likely to affect over a million people each year in the United States [11]. In addition, the costs associated with adverse events were substantial which further underscored the need for investment in efforts to prevent medication errors [12]. Analysis of causal relationships has shown that many errors could be prevented if regulation and policies were well designed and implemented; accordingly, several guidelines for preventing medication errors have been proposed as standards of care [13-20].

To enhance the safety of high-dose chemotherapy administration, the Executive and Practice Committees of The American Society for Blood and Marrow Transplantation (ASBMT) designed a questionnaire to evaluate chemotherapy practices in the United States during 1989-1994. Our hypothesis was that overdoses were associated with identifiable

3

patterns of practice. The study was designed to meet the following objectives: (1) investigate the nature and frequency of overdose errors; (2) describe current safeguard systems in transplant centers; (3) determine whether the absence of certain safeguards was related to overdose errors; (4) determine whether center characteristics were related to errors or practice policy and (5) describe planned policy and practice modifications.

METHODS

Transplant Centers

Pediatric and adult blood and marrow transplant units in the United States were identified from the International Bone Marrow Transplant Registry (IBMTR) and the Autologous Blood and Marrow Transplant Registry-North American (ABMTR). The IBMTR has collected data from over 300 institutions performing allogeneic marrow transplants worldwide since 1972. In 1991, the ABMTR began collecting data on transplants using autologous marrow and /or blood cells done performed in North America. These lists were further updated by members of the Executive and Clinical Practice Committees of ASBMT. A total of 176 centers were identified in 44 states. The eight states with the greatest number of transplant centers were California (24), New York (13), Texas (11), Illinois (11), Florida (9), Ohio (9), Pennsylvania (8), and Massachusetts (7).

Data collection and survey respondents

A self-reporting anonymous form surveyed center attributes, clinical practices, quality control measures for ordering and delivering chemotherapy, and the circumstances and detection of prior overdose errors (appendix). Areas surveyed included: center characteristics; chemotherapy ordering practices; pharmacy policies; nursing practices;

4

quality control and review; cause and detection of overdoses; and current safeguard systems and plans for modifications. The anonymous questionnaire was mailed to 176 program directors. Six were returned as incorrect center identification or no longer involved in transplantation. Replies were received from 115 (68%) of the 170 centers after a second FAX survey was resent to all centers.

To assess possible sampling biases among respondents, one of the authors (M.M.H.) compared the characteristics of the responses from the 115 anonymous centers with those of a larger sample of US centers using the IBMTR/ABMTR database for the same five year period. Seventy centers participating in one or both Registries at some time over the past seven years could not be included because of incomplete data for the years of the current survey. Many of these are centers either began performing transplants or joined the Registry recently. Thus, a total of 139 programs were included in the database for comparison.

Statistical analysis

Statistical comparisons of our samples with the IBMTR/ABMTR database sample were performed with Chi-square test or Fisher's Exact test if any categories occur very infrequently. Logistic regression was used to analyze the rate of occurrence of overdose errors. Missing or ambiguous responses complicated some analyses. All 115 centers provided information on cases of chemotherapy errors, however 17 centers failed to furnish data on the cumulative number of patients transplanted. Due to the anonymous nature of this survey, we were not able to recover omissions or clarify ambiguous data. We used Rubin's multiple imputation method for missing data, in conjunction with the logistic regression approach, so that cases with partial response could be included [21,22]. Multiple

imputation allows calculation of rate estimates, confidence intervals, and test statistics which are adjusted for the fraction of information missing. Intermediate predictor variables used to generate the multiple imputation values for the five-year transplant totals were the current number of transplant-dedicated beds, number of transplants in 1994, and years of center operation.

We recognized that the time frame (item 1 e, **Appendix**), requesting the cumulative number of transplanted patients, could have been interpreted in several ways. All analyses involving error rates were repeated assuming each of three possible interpretations (i.e. a cumulative total of four, five or six years). Rate estimates varied only slightly under the different assumptions (±1/10,000). Rate estimates presented in the text are the medians of the values computed under each set of assumptions, and confidence intervals represent the smallest intervals spanning all three computed intervals. P-values given for comparisons of error rates in relation to center characteristics are the maximums of the three found under each set of assumptions. All p-values presented are two-sided.

RESULTS

Transplant center characteristics

The majority (83%) of hematopoietic cell transplant programs are located in university or university-affiliated hospitals or academic research centers (**Table 1**). A minority (17%) of centers perform only pediatric transplants. Forty-eight (42%) centers conduct only adult and 46 (41%) centers perform both adult and pediatric transplants. Most programs perform both allogeneic and autologous grafts. One hundred eleven (97%) centers are members of national cancer cooperative groups (CALGB, SWOG, ECOG, CCG, POG), or transplant

6

registries (IBMTR or ABMTR) or both. Sixty-nine (60%) centers including ten community hospitals and 59 university or research centers had an external peer review site visit within the preceding three years. The characteristics of respondents to this survey were also compared with those of centers in the IBMTR/ABMTR databases. More centers reporting to IBMTR/ABMTR databases performed autologous transplants only (11% vs 23%, p=0.01) and used peripheral blood stem cells as the only graft source (2% vs 9%; p=0.02). Center characteristics otherwise did not differ significantly between the two groups for type of center, age range of patient treated, membership status of cancer cooperative groups, and number of dedicated transplant beds (data not shown).

Among 114 respondents reporting the year the program began, the median inaugural year was 1988. Forty-one (36%) programs were started since 1990. Fourteen (12%) programs were founded before 1980, and 59 (52%) programs were founded between 1980-1989 (one not specified). For centers reporting data to IBMTR/ABMTR, 63 (47%) started since 1990 which suggests that new centers may be underrepresented in the ASBMT survey (p=0.08).

A total 7,650 hematopoietic cell transplants in 109 centers (six non responses) were performed in 1994, with the annual number of transplants per center ranging from 2 to 460 (median 45) (**Table 2**). Among 109 reporting centers, 24 (22%) programs performed 1-20 transplants, 65 (60%) performed 21-100 transplants and 20 (18%) performed greater than 100 transplants in 1994. The transplant numbers were compared with those reported to the IBMTR/ABMTR. For the most recent year, the survey sample included fewer small centers and more large centers than the IBMTR/ABMTR sample (p=0.04). Between 1989 and 1994, a

7

total of 22,542 transplants were recorded at the 98 centers responding to this survey (ranging from 2 to 2,586, median 121). However, by considering the 1994 data along with the 1989-1994 totals for centers with incomplete responses, we estimated that a minimum of 24,255 transplants occurred at the 115 participating centers.

Safety practices and quality control

As shown in **Table 3**, 98 (85%) centers used preprinted chemotherapy order sheets. Among the 98 centers, 12 used preprinted orders for some but not all conditioning chemotherapy. A total of 94 centers listed the chemotherapy dose per date in the preprinted orders and 74 centers included the dose per course in the preprinted orders. The reasons given for not using preprinted orders included: treatment off-protocol (seven centers), small accrual protocols (six centers), and new protocols (two centers). Chemotherapy orders were signed by physician assistant, resident, fellow, and attending in 22, 24, 57, and 107 centers, respectively. Among the eight centers where order sheets were not signed by attendings, four required no mandatory co-signatures.

The chemotherapy dose was recalculated in the pharmacy in 106 (92%) centers. Chemotherapy dose verification was performed by one pharmacist in 66, or two pharmacists in 38, or three pharmacists in one center (one not specified). Six centers indicated no dose recalculation by a pharmacist but four of the six utilized computer programs for drug ordering. Sixty-nine (60%) centers operated a computer system for drug ordering and dose limits were set by computer in 22 of the 69 centers. All 115 centers indicated that the chemotherapy dose and drug in bag were identified by nursing staff. Nursing verification of chemotherapy infusions was carried out by two nurses in 66 (57%) centers and one nurse in

8

42 (37%) centers (seven [6%] not specified). Doses were verified against orders in 111 (97%) centers and against the protocol in 73 (64%) centers by nurses. Patient identification and dose verification against orders were not performed in, respectively, five and three centers.

Among the 98 centers using preprinted orders, 15 have one, 71 have two-four and 11 centers have five-six quality control reviews of the order forms (one not specified). Reviewers included primary investigators (76 centers), medical directors (69 centers), pharmacy directors (33 centers), nursing directors (24 centers), research nurses (43 centers) and others (23 centers). Multidisciplinary standard practice committees (72 centers [63%]) and transplant quality assurance committees (76 centers [66%]) were common components of quality control. Other committee or group reviews included medical advisory and staff conferences, policy and procedures, critical care, infection control, and transfusion committees. Eighty-seven centers (78%) had all protocols reviewed by Institutional Review Board (IRB). Twenty-five centers, including 18 University/affiliated centers, six community hospitals, and one of unspecified type, indicated that not all stem cell transplant protocols were reviewed by the IRB. Exemptions included transplants considered as standard treatments (16 centers), non-research protocols (four centers), and other reasons (three centers).

Nature and frequency of overdose errors

Fifteen centers reported a total of 18 individuals who received overdoses of high-dose therapy between 1989 and 1994. Twelve centers reported one case each and three reported two cases. The circumstances surrounding the errors, methods of detection and subsequent policy revisions are detailed in **Table 4**. The overdosed agents included cisplatin (n=3),

carboplatin (n=2), busulfan (n=2), cytosine arabinoside (n=2), cyclophosphamide (n=2), interleukin-2 (n=2), and doxorubicin, adriamycin, vincristine, methotrexate, and the combination of thiotepa/carboplatin/etoposide (one each). Cumulative drug doses given for the daily dose (six cases) and nursing infusion errors (six cases) were the most common type of error followed by ambiguous orders without attending co-signatures (two cases), new protocols without preprinted orders (two cases), pharmacy or staff errors (one each). Three centers (cases 14, 15, and 17) using computer programs for dose limitations had errors in physician orders (two cases) or pharmacy verification (one case). Errors prompted policy revisions at ten centers: use of preprinted orders, verification of order against protocol, order listing of maximum drug dose, limiting of orders to daily dose, verification of all chemotherapy orders by attending physicians, pharmacists and nurses, and increased training and education. In addition, seven centers (nine cases) described their revision as reinforcing multidisciplinary checkpoints.

The overall rate of chemotherapy overdoses for the five-year period surveyed was 0.06%, or 6 cases in 10,000 transplants, with 95% confidence limits of 0.03%-0.11%. Univariate regression analyses detected a lower error rate among large centers (greater than 100 transplants in 1994) than among medium-sized centers (21-100 transplants) (p=0.03), however, there was no evidence that small centers (1-20 transplants) differed from medium-sized ones (p=0.99). Centers in operation before 1990 also had a statistically significantly lower error rate (p < 0.01). These two findings are closely linked because the older centers are also generally larger. Results also suggest a trend that centers reporting verification by two nurses rather than one might have a lower error rate (p=0.11). Other center characteristics which did not show statistical association with error rates were:

10

community vs. university affiliated institution/research center and presence of computerized drug ordering (p >0.35).

DISCUSSION

This study profiles transplant programs and safety practices for high-dose chemotherapy administration in the United States. Patients were treated in a variety of settings ranging from community hospitals to university/research centers throughout the nation. Because hematopoietic cell transplantation is a complex and expensive technology, factors such as geographical, social, ethnic, or financial/payer diversities may influence the distribution of transplant centers [23-25]. The 68% response rate to this anonymous survey was high given the fact only one blinded follow-up reminder was sent to all program directors. This response rate was similar to return rates in many unblinded surveys [26,27]. The comparison with the IBMTR/ABMTR database helps to address the potential for selection bias in the responding sample. Smaller or new centers may not have responded to this survey as readily as older and/or larger ones. The registry data-base consistently comprises about 50% of auto-transplants and 40% allo-transplants in the United States. Their representations were evaluated and confirmed independently [28, and unpublished data]. Even though the transplant registries do not receive all the transplant reports, the total number of transplants in the United Stated can be estimated. About 50,000 transplants (18,000 allogeneic and 32,000 autologous) were performed between 1989 and 1994, and 10,000-12,000 transplants (3-4,000 allogeneic and 7-8,000 autologous) in 1994. Thus, the total number of transplants reported here for 1994 reflects a significant proportion (64-77%) of hematopoietic transplants performed in the United States.

11

The reported Overdose rate, 6 cases/10,000 transplants in a five-year period, is lower than overall medication error rates reported in the Harvard Medical Practice Study. [7]. In that retrospective study with a sample size of 30,195 hospitalized patients, the adverse event rate was 3.7% and drug complications were the most common type of adverse events (19% of total) which could be translated into a rate of 7 cases/1000 patients. It should be emphasized that a direct comparison of our results with this reported error rate is difficult. Our survey specifically focused on high-dose chemotherapy overdose which represents one of the most severe forms of adverse drug events but did not address the issue of overall drug related adverse events. It is possible that non-chemotherapy medication errors also occurred but that information was not provided. Moreover, while the self-reporting survey is a method of error identification frequently used in the literature, a disadvantage is that errors are not reported unless discovered. Accordingly, self-reported error rates tend to be lower than the actual rates. Despite the limitations of this approach, the purpose of our survey was to provide an opportunity for self-examination of practices. In addition, it provided a method of collecting and analyzing data on medication errors in settings where treatments were often new and intensive with overdoses potentially resulting in serious consequences. Besides self-reporting, alternative strategies for the study of medical injury include prospective tracking of particular procedures or after the fact analysis of medical records. These methods of detecting error are also far from perfect. A recent report has suggested a new approach for studying adverse events in medical care [29]. Using ethnographers participating in all medical rounds and conferences to record adverse events during patient care discussions, the rate of adverse events was found to be 17.7% in a study of 1047 patients, which was considerably higher than the 3.7% reported in the Harvard study.

In this survey, cumulative drug doses given for the daily dose and nursing infusion mistakes were the most common type of errors; however, overdoses occurred at every step between the process of ordering and administration. Error rates were higher among newer centers established after 1990 which also tended to be smaller units, suggesting that centers with more experience in high-dose chemotherapy may be more likely to avoid errors. Alternatively, errors may have been recognized in the past and safeguards subsequently strengthened. We could not find individual safeguard measures which were statistically associated with reduced rates of error. Center variation in marrow or blood stem cell transplantation outcome is more difficult to study, due in part to wide variations in treatment protocols and patient selection. While data from this survey showed that larger and more experienced centers have lower reported error rates, these findings should be interpreted with caution and should not be used as surrogate markers of hospital performance or outcome since variables associated with voluntary reporting make comparisons between institutions difficult [30]. Safety practices for chemotherapy administration were studied at the physician, pharmacist and nursing levels. While all centers have procedures in place to prevent chemotherapy error, the degree of thoroughness differed. Computer programs for drug orders and dose limits may have prevented errors; however, this issue was not addressed by this survey. Importantly, some errors occurred even with computer monitoring in place. Dose verification against protocols as well as confirmation of the patient's weight and body surface area were less commonly performed. Twenty-four centers noted that residents wrote chemotherapy orders which were countersigned by either fellows or attendings. Interestingly, a recent survey of standard chemotherapy administration by 150 members of the American Society of Clinical Oncology suggested that very few

13

programs had chemotherapy orders written by interns or residents. The incidence of medication error was not addressed in that survey [27].

Our findings are consistent with earlier reports that medication errors frequently occur as a result of multi-system failures. Adverse events and iatrogenic injuries are serious and costly complications of health care and represent a wide range of potential events or errors. Many adverse drug events analyzed in the Harvard study were complex in nature. Specifically, episodes were attributed to various problems of process or unique errors caused many categories of adverse drug events. With a systemic approach, errors can be reduced by examining elements and interrelationships of the safety structure [17,18,31,32]. The magnitude of medical adverse events is probably underestimated since most studies have focused only on injury. Error rates have been distressingly high when errors were specifically audited. For example, autopsy studies indicated high rates (35%-40%) of missed diagnosis causing death [33-35]. The annual national cost of such drug-related morbidity and mortality has been estimated as $76.6 billion, with the majority ($47 billion) related to hospital admissions associated with drug therapy [12]. Two recent reports have quantified the additional resource utilization associated with these events [36,37]. Data from the prevention study suggested the annual costs attributable to all adverse events and preventable events for a 700-bed teaching hospital were $5.6 million and $2.8 million, respectively.

Marrow and peripheral blood stem cell transplants are increasingly employed to treat an enlarging array of diseases. This in turn has led to a large number of centers established since 1990. It is possible that some newer centers may have less established safeguard

systems. Importantly, no standard practice guidelines have been previously formulated for transplantation. To reduce errors in conventional chemotherapy, the American Society of Health-Systems Pharmacists has promoted several measures, including certification examinations for oncology-trained pharmacists [19,20]. Based upon the findings of this survey and the experience in the literature, the American Society for Blood and Marrow Transplantation proposes specific guidelines for high-dose chemotherapy administration outlined in **Table 5**. These guidelines emphasize the need for a multidisciplinary approach to standardizing safety practice and apply equally to transplant centers of all types, sizes and experience. Medication errors should be monitored at the institutional level so that similar incidents can be prevented in the future. In addition, medication errors or potential errors may be reported in confidence to the MEDWATCH program of the Food and Drug Administration (tel 1-800-FDA-1088 or fax the MEDWATCH form to 1-800-FDA-0178). Future efforts at error prevention may be further aided by enhanced monitoring and advances in bioinformatics. Use of electronic medical records and computerized physician ordering will eliminate confusing handwritten records and implementation of bar-coding of medications and patient identification will positively identify patients and treatments [38].

In conclusion, this self-reporting survey of administration of high-dose chemotherapy characterized the current practices and safety measures in a large cohort of blood and marrow transplant centers. Common themes to these errors were cumulative drug doses given as a daily dose and nursing infusion errors. Guidelines are proposed to reduce system-wide errors and further safeguard the administration of high-dose chemotherapy and hematopoietic cell transplantation.

Acknowledgments

REFERENCES

1. Thomas ED. Marrow transplantation for malignant diseases. J Clin Oncol 1983; 9:517-531.

2. Armitage JO. Bone marrow transplantation. N Engl J Med 1994; 330:827-38.

3. Walters MC, Patience M, Leisenring W, et al. Bone marrow transplantation for sickle cell disease. N Engl J Med 1996; 335:369-76.

4. Knox RA. Dana-Farber head quits 2d post-news changes. Boston Globe, May 26, 1995.

5. Altman LK. Medical errors bring calls for change. New York Times, July 18, 1995.

6. Erikson J. How safe are the safeguards? A death at Dana-Farber triggers soul searching at cancer centers. Oncology Times. Vol XVII No.7, July 1995.

7. Leape LL, Brennan TA, Laird NM, et al. The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. N Engl J Med 1991; 324:377-84.

8. Linden JV, Kaplan HS. Transfusion errors: causes and effects. Transfus Med Rev 1994; 8: 169-83.

9. Donchin Y, Gopher D, Olin M, et al. A look into the nature and causes of human errors in the intensive care unit. Crit Care Med 1995; 23:294-300.

10. Lagasse RS, Steinberg ES, Katz RI, Saubermann AJ. Defining quality of perioperative care by statistical process control of adverse outcomes. Anesthesiology 1995; 82: 1181-8.

11. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. N Engl J Med 1991; 324:370-6.

12. Johnson JA, Bootman JL. Drug-related morbidity and mortality: a cost-of-illness model. Arch Intern Med 1995; 155: 1949-6.

13. Leape LL, Lawthers AG, Brennan TA, Johnson WG. Preventing medical injury. Qual Rev Bull 1993; 19:144-9.

14. American Society of Hospital Pharmacists. ASHP guidelines on preventing medication errors in hospitals. Am J Hosp Pharm 1993; 50:305-14.

15. Bradbury K, Wang J, Haskins G, Meh B. Prevention of medication errors. Developing a continuous-quality-improvement approach. Mt Sinai J Med 1993; 60:379-86.

16. Cohen MR, Senders J, Davis NM. Twelve ways to prevent medication errors. Nursing 1994; 24:34-41.

17. Leape LL, Bates DW, Cullen DJ, et al. Systems analysis of adverse drug events. JAMA 1995; 274: 35-43.

18. Bates DW, Cullen DJ, Laird NM, et al. Incidence of adverse drug events and potential adverse drug events. Implications for prevention. JAMA 1995; 274:29-34.

19. Cohen MR, Anderson RW, Attilio RM, Green L, Muller RJ, Pruemer JM.:Preventing medication errors in cancer chemotherapy. Am J Health Syst Pharm 1996; 53:737-46.

20. Bates DW, Burrows AM, Grossman DGS, et al. Top priority actions for preventing adverse drug events in hospitals. Am J Health Syst Pharm 1996; 53: 747-51.

21. Rubin, Donald B. Multiple Imputation for Nonresponse in Surveys, John Wiley & Sons, NewYork. 1987.

22. Rubin, Donald B. Multiple imputation after 18+ years. J Am Stat Assoc 1996; 91: 473-87.

23. Goldman JM. Bone marrow transplantation in Europe-Can the geographical differences be explained? J Intern Med ; 233:311-3.

24. Silberman G, Crosse MG, Peterson EA, et al. Availability and appropriateness of allogeneic bone marrow transplantation for chronic myeloid leukemia in ten countries. N Engl J Med 1994; 331:1063-7.

25. Schulman KA. Economics of bone marrow transplantation. J Clin Oncol 1996; 14:1409-10.

26. Armstrong BK, White E, Saracci R. Response rates and their maximization. Monographs in Epidemiology and Biostatistics 1992; 21:294-321.

27. Fischer DS, Alfano S, Knobf MT, Donovan C, Beaulieu N. Improving the cancer chemotherapy use process. J Clin Oncol 1996; 14:3148-55.

28. Rowlings PA, Passweg JR, Armitage JO, et al. Report from the International Bone Marrow Transplant Registry and the Autologous Blood and Marrow Transplant Registry-North America. Clin Transpl 1994; 6 :87-98.

29. Andrews LB, Stocking C, Krizek T, et al. An alternative strategy for studying adverse events in medical care. Lancet 1997; 349: 309-13.

30. van Leeuwen DH. Are medication error rates useful as comparative measures of organizational performance? Jt Comm J Qual Improv 1994; 20:192-9.

31. Bates DW, Boyle DL, Vaner Vliet MB, Schneider J, Leape LL. Relationship between medication errors and adverse drug events. J Gen Intern Med 1995; 10:199-205.

32. Kahn KL. Above all "Do No Harm" How shall we avoid errors in medicine? JAMA 1995; 274:75-6.

33. Anderson RE, Hill RB, Key CR. The sensitivity and specificity of clinical diagnostics during five decades: toward an understanding of necessary fallibility. JAMA 1989; 261: 1610-11.

34. Goldman L, Sayson R, Robbins S, Conn LH, Bettman M, Weissberg M. The value of the autopsy in the three medical eras. N Engl J Med 1983; 308:1000-5.

35. Cameron HM, McGoogan E. A prospective study of 1,152 hospital autopsies, I: Inaccuracies in death certification. J Pathol 1981; 133: 273-83.

36. Bates DW, Spell N, Cullen DJ, et al. The costs of adverse drug events in hospitalized patients. JAMA 1997; 277:307-11.

37. Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients-excess length of stay, extra costs, and attributable mortality. JAMA 1997; 277:301-6.

38. Leape LL. Examinig errors in health care: Developing a prevention, education, and research agenda. Conference presentation, Rancho Mirage, CA, Oct. 13-15, 1996.

Table 1

Characteristics of 115 Transplant Programs

Type of center (n=113)	Number (%)
University hospital, affilliated hospital or research center	94 (83%)
Community hospital	19 (17%)
Type of transplant	
Graft source (n=115)	
Both blood and marrow	109 (95%)
Peripheral blood stem cell only	2 (2%)
Bone marrow only	4 (3%)
Donor (n=114)	
Both autologous and allogeneic (no unrelated)	51 (45%)
Autologous, allogeneic and unrelated	49 (43%)
Autologous only	13 (11%)
Allogeneic only	1 (1%)
Type of patients treated (n=113)	
Both adult and pediatric patients	46 (41%)
Adult patients only	48 (42%)
Pediatric patients only	19 (17%)
Member of cancer cooperative groups¶ or transplant registry (n=115)	
Cooperative Groups, ABMTR and IBMTR	66 (58%)
Cooperative Groups and ABMTR	15 (13%)
Cooperative Groups and IBMTR	7 (6%)
ABMTR and IBMTR	6 (5%)
Cooperative Groups only	10 (9%)
ABMTR	6 (5%)
IBMTR	1 (1%)
None	4 (3%)
Number of dedicated transplant beds (n=112)	
1-5	30 (27%)
6-10	45 (40%)
11-20	23 (21%)
21-30	8 (7%)
31-60	6 (5%)
Peer review site visit within last 3 years (n=115)	
NIH	30*
FDA	10*
Cooperative Groups	25*
Others §	17*
None	46 (40%)

¶ The Cooperative Groups included Cancer and Leukemia Group B (CALGB), Southwest Oncology Group (SWOG), Eastern Cooperative Oncology Group (ECOG), Puget sound Oncology Group (POG), and Children Cancer Groups (CCG).
§ Other mechanisms included by State, National Surgical Adjuvant Breast and Bowel Projects (NASBP), National Marrow Donor Program (NMDP), American Association of Blood Banks (AABB), College of American Pathologists (CAP), American Society for Histocompatibility (ASHI), or panel of experts/cancer center review. Eleven centers were reviewed by two or more groups.
* Some programs indicated more than one review mechanism, therefore, percentage is not given.

Table 2

Number of Transplants in 1994 and 1989-1994

Transplants	1994 Center number (%)		Transplants	1989-1994 Center number (%)	
	ASBMT survey	IBMTR/ABMTR		ASBMT survey	IBMTR/ABMTR
1-5	5 (5%)	10 (7%)	1-50	28 (29%)	39 (28%)
6-10	6 (6%)	19 (14%)	51-100	14 (14%)	27 (19%)
11-20	13 (12%)	30 (22%)	101-200	28 (29%)	30 (22%)
21-40	26 (24%)	27 (19%)	201-400	17 (17%)	29 (21%)
41-60	21 (19%)	21 (15%)	>401	11 (11%)	14 (10%)
61-100	18 (16%)	21 (15%)	Not specified	17	
101-200	13 (12%)	8 (6%)	Total number of center	115 (100%)	139 (100%)
>201	7 (6%)	3 (2%)			
Not specified	6				
Total number of center	115 (100%)	139 (100%)			
	p=0.04			p=0.65	

ASBMT

Table 3

Safety Practices for High-dose Chemotherapy Administration in 115 Centers

	Routinely used (%)	Not used (%)	Not specified
Chemotherapy orders			
Preprinted chemotherapy orders used	98† (85%)	17 (15%)	0
Preprinted orders used for each drug¶	84	12†	2
Dates of chemotherapy¶	96	1	1
Dose per day¶	94	3	1
Dose per course¶	74	23	1
Protocol drug dose typed on the orders	93 (81%)	19 (17%)	3
Protocol number specified on the orders	74 (64%)	36 (31%)	5
Chemotherapy infusions			
Pharmacy verification			
Pharmacist recalculates dose	106 (92%)	6 (5%)	3
Dose verified against protocol	87# (76%)	23 (20%)	5
Computerized drug order	69* (60%)	45 (39%)	1
Program sets dose limit§	22* (32%)	43 (62%)	3
Nursing verification			
Dose and drug in bag verified	115 (100%)	0 (0%)	0
Dose verified against orders	111 (97%)	3 (2%)	1
Patient identification verified	109 (95%)	5 (4%)	1
Dose verified against protocol	73 (64%)	41(35%)	1
Patient weight and body surface area verified	90 (78%)	23 (20%)	2

† See text.
¶ Based on the 98 centers using any preprinted orders.
§ Based on the 69 centers using computerized drug orders.
* One program indicated that only some chemotherapy was computerized and has dose limit set.
# One program indicated that only some chemotherapy doses were verified against protocol.

Table 4

High Dose Chemotherapy Overdose Errors and Policy Changes

Cases	Type of Errors*	Drug	Method of Detection	Policy Change	Reinforced Safeguard Systems
1	Cumulative dose given for daily dose (3-fold overdose)	Doxorubicin	Nurse recognized errors later	yes	Pharmacy verify protocols
2	Cumulative dose given for daily dose (4-fold overdose)	Cisplatin	Review of chart/toxicity	yes	Use preprinted orders; pharmacist verify doses; dedicated nurses on transplant
3	Cumulative dose given for daily dose	Cisplatin	Pharmacy detected error later	yes	Multidisciplinary checkpoints; list maximum drug doses for treatments
4	Cumulative dose given for daily dose	Cisplatin	Pharmacy detected error later	yes	Multidisciplinary checkpoints; list maximum drug doses for treatments
5	Cumulative dose given for daily dose	Adriamycin	Pharmacy detected error later	yes	Limit orders to daily dosing
6	Cumulative dose given for daily dose, no attending co-signature (3-fold overdose)	Carboplatin	Pharmacy detected error later	no	Multidisciplinary checkpoints; new protocol orientation; attending co-signs orders
7	Nursing error (Bid dose given concurrently, 2-fold overdose)	Cytosine arabinoside	Physician monitoring	no	Multidisciplinary checkpoints
8	Nursing error (Bid dose given concurrently, 2-fold overdose)	Cytosine arabinoside	Physician monitoring	no	Multidisciplinary checkpoints
9	Nursing error (24hr infusion given in 6hr)	Cyclophosphamide	Nurse recognized errors later	no	Multidisciplinary checkpoints
10	Nursing error and Pharmacy error	Busulfan	Nurse recognized errors later	no	Multidisciplinary checkpoints
11	Nursing error	Interleukin-2	Pharmacy detected error later	no	Verify orders and doses against protocols by pharmacists
12	Nursing error	Interleukin-2	Pharmacy detected error later	no	Verify orders and doses against protocols by pharmacists
13	Ambiguous orders and no attending co-signature	Carboplatin	Laboratory monitoring, increase creatinine	yes	Review preprinted orders; attending co-signs orders
14	Ambiguous orders and no attending co-signature	Vincristine	Clinical toxicity	yes	Attending co-signs orders
15	New protocol and no preprinted orders	Cyclophosphamide	Review of chart	yes	Use preprinted orders; increase awareness
16	New protocol and new fellow	Thiotepa/Carboplatin /Etoposide	Attending detected error	no	Multidisciplinary checkpoints
17	Pharmacy error	Methotrexate	Clinical toxicity	yes	Multidisciplinary checkpoints; review chemotherapy policies
18	Unable to check Busulfan blood level	Busulfan	Clinical toxicity	yes	Centralized incident reports; attending verify all orders

* Details varied among centers, all description provided was included.

ASBMT

Table 5

ASBMT Guideline for High-Dose Chemotherapy Administration

Physician Orders

Use preprinted orders.

Specify protocol number and name of study on the orders.

Specify daily drug dose and specific chemotherapy dates for all drugs.

Physician Procedures

Physician verifies that two staff members independently confirm patients' height and weight.

Attending Physician verifies the name, and protocol number, and recalculates the drug dose.

Attending Physician co-signs all chemotherapy orders.

Pharmacist Procedures

Pharmacist verifies the name, protocol, and recalculates the drug dose.

Cumulative dose is recalculated and compared to the protocol maximum total cumulative dose.

Nursing Procedures

Two nurses establish the patient identity and the drug for administration.

Nurse verifies drug doses against both the order sheet and the protocol.

Institutional Procedures

Multidiciplinary review of new or revised protocols and preprinted orders.

Continuing staff education of chemotherapy safeguards.

Appendix

ASBMT
ANONYMOUS QUESTIONNAIRE
(forms will be destroyed and only pooled data kept)

1.   Center Specifics

a.   Type of transplants (check all):
        1) Bone marrow   Peripheral blood
        2) Adult   Pediatric
        3) Autologous   Allogeneic   Unrelated

b.   Type of center: University Hospital   Research Center
                Community Hospital   University Affiliated: yes   no
c.   Year program started:

d.   Number of dedicated transplant beds:

e.   Number of transplants in: 1994   1989-1994

f.   Member of cancer group or transplant registry (check all):
            1) Cooperative Group (specify)   IBMTR   ABMTR

g.   Peer review site visit within last 3 years by:
            1) NIH   FDA   Other (Specify)

2.   Chemotherapy Orders

a.   Order sheets signed by (check all):
        Resident   Fellow   PA   Attending

b.   Order sheets require mandatory cosign by:
        Fellow   Attending   Not cosigned

c.   Are preprinted chemotherapy orders used?
            1) Yes   No
            2) If yes, in what percent of patients?   %
            3) Which patients do not have preprinted orders?

d.   Are preprinted orders used for each drug?   Yes   No
            1) If not, which chemotherapy is exempt?

e.   Is the protocol number specified on the orders?   Yes   No

f.   Is the drug dose (mg/m2 or mg/kg) from the specific protocol typed on the orders?
            1) Yes   No

g.   Do preprinted orders provide specific space for:
        1) Dates of chemotherapy?   Yes   No
        2) Dose per day?   Yes   No
        3) Dose per course?   Yes   No

3.   Chemotherapy Infusions: Pharmacy

a.   Is drug ordering computerized?   Yes   No
b.   If so, does the program set dose limits?   Yes   No
c.   Does the pharmacist recalculate the dose?   Yes   No

d. Does the pharmacist verify against protocol?   Yes   No
e. Verification by: one pharmacist   two pharmacists

4. Chemotherapy Infusions: Nursing

a.	Does the nurse verify patient ID?	Yes	No
b.	Does the nurse verify dose and drug in bag?	Yes	No
c.	Does the nurse verify dose against orders?	Yes	No
d.	Does the nurse verify dose against protocol?	Yes	No
e.	Does the nurse verify weight/BSA of patient?	Yes	No
f.	Verification by: one nurse two nurses		

5. Quality Control

a. Who reviews preprinted orders and revisions? (check all):
    Principal investigator   Medical Director   Research Nurse
    Pharmacy Director   Nursing Director   Other (specify)

b. Do you have an active, multidisciplinary Standard Practice Committee to update/revise orders and transplant practice? Yes   No

c. Do you have a transplant Quality Assurance Committee? Yes   No

d. Do other committees/groups review transplant practice? (describe)

e. Does the IRB review all protocols? Yes   No
    If no, which are exempt?

f. Who, how and when do you monitor for regimen-related toxicities?

g. Over the last 5 years, has there been inadvertent administration of higher than planned doses of chemotherapy? Yes   No
    1) How many patients?
    2) Which agents?
    3) Why did it occur (be specific):
    4) How was it detected?

6. Systems Design
a. What aspects of your system are the strongest safeguards?
b. What are areas of concern for safety?
c. Are you planning any change in your policies? Yes   No
If yes, specify:

Editor   July 11, 1997
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen, MD., Ph.D.   Kristy Seidel, MS.

James O. Armitage, MD.   Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.   Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.   Paul L. Weiden, MD.

Karen S. Antman, MD.   Richard E. Champlin, MD.

John H. Kersey, MD.   Keith M. Sullivan, MD.

**FRED
HUTCHINSON
CANCER
RESEARCH
CENTER**

Editor   July 11, 1997
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen, MD., Ph.D.   Kristy Seidel, MS.

James O. Armitage, MD.   Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.   Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.   Paul L. Weiden, MD.

Karen S. Antman, MD.   Richard E. Champlin, MD.

John H. Kersey, MD.   Keith M. Sullivan, MD.

**FRED
HUTCHINSON
CANCER
RESEARCH
CENTER**

July 11, 1997

Editor
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen, MD., Ph.D.   Kristy Seidel, MS.

James O. Armitage, MD.   Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.   Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.   Paul L. Weiden, MD.

Karen S. Antman, MD.   Richard E. Champlin, MD,

John H. Kersey, MD.   Keith M. Sullivan, MD.

1124 Columbia Street   Seattle, Washington 98104-2092   206-667-5000

TOTAL P.02

**FRED
HUTCHINSON
CANCER
RESEARCH
CENTER**

Fax to:
— 206-667-2147

Editor
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

July 11, 1997

From: Karen Antman

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen, MD., Ph.D.

Kristy Seidel, MS.

James O. Armitage, MD.

Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.

Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.

Paul L. Weiden, MD.

Karen S. Antman, MD.

Richard E. Champlin, MD.

John H. Kersey, MD.

Keith M. Sullivan, MD.

**FRED
HUTCHINSON
CANCER
RESEARCH
CENTER**

Editor   July 11, 1997
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen, MD., Ph.D.   Kristy Seidel, MS.

James O. Armitage, MD.   Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.   Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.   Paul L. Weiden, MD.

Karen S. Antman, MD.   Richard E. Champlin, MD.

John H. Kersey, MD.   Keith M. Sullivan, MD.

FRED
HUTCHINSON
CANCER
RESEARCH
CENTER

Editor   July 11, 1997
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen. MD., Ph.D.   Kristy Seidel, MS.

James O. Armitage, MD.   Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.   Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.   Paul L. Weiden, MD.

Karen S. Antman, MD.   Richard E. Champlin, MD.

John H. Kersey, MD.   Keith M. Sullivan, MD.

1124 Columbia Street Seattle, Washington 98104-2092 206·667·5000

FRED HUTCHINSON CANCER RESEARCH CENTER

July 11, 1997

Editor
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled. "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center. 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen, MD., Ph.D.   Kristy Seidel, MS.

James O. Armitage, MD.   Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.   Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.   Paul L. Weiden, MD.

Karen S. Antman, MD.   Richard E. Champlin, MD.

John H. Kersey, MD.   Keith M. Sullivan, MD.

FRED
HUTCHINSON
CANCER
RESEARCH
CENTER

July 11, 1997

Editor
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen. MD., Ph.D.

James O. Armitage, MD.

Frederick R. Appelbaum, MD.

Elizabeth J. Shpall, MD.

Karen S. Antman, MD.

John H. Kersey, MD.

Kristy Seidel, MS.

Joseph W. Fay, MD.

Mary M. Horowitz, MD, MS.

Paul L. Weiden, MD.

Richard E. Champlin, MD.

Keith M. Sullivan, MD.

Editor   July 11, 1997
New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094

Dear Editors:

Enclosed for consideration of publication in the *Journal* is the enclosed manuscript entitled, "Safeguarding the administration of high-dose chemotherapy: A national practice survey by the American Society for Blood and Marrow Transplantation". Given the high visibility of recent reports of medical errors, this study may have wide readership interest.

Correspondence concerning the manuscript should be addressed to Dr. Sullivan at the Fred Hutchinson Cancer Research Center, 1124 Columbia St. Seattle, WA 98104. The final manuscript has been seen and approved by all contributing authors.

Sincerely,

Chien-Shing Chen, MD., Ph.D.   Kristy Seidel, MS.

James O. Armitage, MD.   Joseph W. Fay, MD.

Frederick R. Appelbaum, MD.   Mary M. Horowitz, MD, MS.

Elizabeth J. Shpall, MD.   Paul L. Weiden, MD.

Karen S. Antman, MD.   Richard E. Champlin, MD.

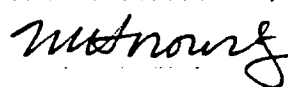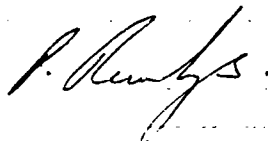John H. Kersey, MD.   Keith M. Sullivan, MD.

HIGH-DOSE CHEMOTHERAPY AND BLOOD OR BONE MARROW TRANSPLANT FOR PATIENTS WITH HIGH-RISK BREAST CANCER

Dr. Philip Rowlings, Dr. Karen Antman, Dr. James Armitage and Dr. Mary Horowitz

for the Breast Cancer Working Committee of the
Autologous Blood and Marrow Transplant Registry (ABMTR),
Health Policy Institute, Medical College of Wisconsin, Milwaukee, WI 53226

Autotransplantation, a recently developed cancer treatment, involves giving very high doses of chemotherapy followed by bone marrow stem cells collected from the patient before high-dose treatment. Stem cells are needed because high-dose anti-cancer drugs destroy normal bone marrow stem cells, which produce all circulating blood cells. Stem cells are collected directly from bone marrow (usually from the hip bone) or from blood. When collected from bone marrow, the treatment is called a bone marrow transplant; when collected from blood it is a blood cell or peripheral blood stem cell transplant. The ABMTR has information on >9000 women receiving autotransplants for breast cancer from 1989-1996.

Review of ABMTR data reveals that breast cancer is the disease most commonly treated with blood or bone marrow transplantation in North America. More and more women receive autotransplants early after diagnosis with about half treated for localized disease and half for disease which has spread (metastatic). Blood-derived stem cells are used more commonly than bone marrow. Safety of autotransplants improved dramatically since 1989, with the procedure-related death rate decreasing from >15% to <5%. Transplant results differ depending on stage of disease at time of transplant. Woman with stage 2 or 3 disease have higher survival rates than women with metastatic disease. Women whose breast cancer responded to traditional chemotherapy before transplant do better after transplant than women whose cancers were unresponsive. The ABMTR database, which has comprehensive pre- and posttransplant information, is a unique resource for investigators planning and interpreting clinical trials, health-care agencies assessing technology and physicians and patients making treatment decisions.

HIGH-DOSE CHEMOTHERAPY WITH AUTOLOGOUS HEMATOPOIETIC STEM-CELL SUPPORT FOR HIGH-RISK PRIMARY AND METASTATIC BREAST CANCER

Dr. Philip Rowlings, Dr. Karen Antman, Dr. James Armitage and Dr. Mary Horowitz

for the Breast Cancer Working Committee of the
Autologous Blood and Marrow Transplant Registry (ABMTR),
Health Policy Institute, Medical College of Wisconsin, Milwaukee, WI 53226

Breast cancer is the most common cancer and the second most common cause of cancer deaths in American women. High-dose chemotherapy with autologous hematopoietic stem cell support (autotransplant) is increasingly used to treat breast cancer in women at high risk of persistent or recurrent disease. Most reports of autotransplants describe results in relatively few women. Results of cooperative group randomized trials comparing autotransplants to conventional therapy will not be available for some years and are not designed to address many important issues including patient selection and optimal regimens. To make data regarding autotransplants for women with breast cancer readily available for multiple studies, a large representative database was established by the Statistical Center of the ABMTR. The Statistical Center uses this database to follow trends in numbers of autotransplants performed for breast cancer, characteristics of women receiving autotransplants and overall outcome. ABMTR Working Committees use the data to perform sophisticated analyses of prognostic factors and therapeutic strategies. Additionally, the data are available to investigators planning and evaluating clinical trials, health care agencies evaluating the technology, and physicians and patients making treatment decisions. This report summarizes results of autotransplants in more than 9000 consecutive women receiving autotransplants at over 170 centers between 1989 and 1996.

By 1993-94, breast cancer was the single most common indication for hematopoietic stem cell transplant (autologous or allogeneic). Changes in patient-, disease- and transplant-related characteristics and early mortality are presented in Table 1. Significant trends include increasing use of autotransplants for high-risk primary disease rather than metastatic disease ($p < 0.00001$) and increasing use of blood-derived rather than marrow-derived hematopoietic stem cells ($p < 0.00001$). One hundred-day mortality decreased from 17% to 4% ($p < 0.0001$).

Keywords: High-dose Therapy, Autotransplant, Blood Stem Cell and Bone Marrow Transplant, Prognostic Factors

Characteristics of patients receiving autotransplants for breast cancer from 1989-96 reported to the ABMTR.

	1989-90	1991-2	1993-4	1995-6
Number of patients transplanted	600	1900	3000	4200
Median age, yrs (range)	43 (23-66)	44 (19-72)	45 (24-70)	46 (22-73)
Disease stage at transplant				
High-risk primary	13%	30%	36%	47%
Metastatic	87%	70%	64%	53%
Graft type				
Bone Marrow	78%	46%	23%	8%
Peripheral Blood Stem Cell	16%	26%	53%	78%
BM + PBSC	6%	28%	24%	14%
100-day mortality	17%	7%	4%	4%

Survival following autotransplant for metastatic disease is predicted by tumor response to standard dose chemotherapy. Three-year probabilities of survival (95% confidence interval) for patients in complete remission, in partial remission and with non-responsive disease at transplant are 46 (40-52)%, 29 (25-33)% and 16 (12-20)%, respectively. Progression-free survivals are 32 (27-37)%, 13 (9-17)% and 7 (4-10)%, respectively. Multivariate analyses indicate that, in addition to sensitivity to standard dose chemotherapy, estrogen receptor positivity, higher Karnofsky performance score (90-100 vs <90) and bone-only metastases (compared to soft tissue or visceral metastases) are associated with an improved progression-free survival (all, p < 0.0001).

Survival following autotransplant for high-risk primary disease varies according to the presence of inflammatory disease. Three-year probabilities of survival are 74 (68-80)%, 70 (63-77)% and 52 (12-20)%, respectively for stage 2, 3 and inflammatory breast cancer. Progression-free survivals are 65 (59-71)%, 60 (53-67)% and 42 (31-53)%, respectively. Preliminary analyses suggest that posttransplant tamoxifen for estrogen receptor positive disease and local radiation improve results.

In conclusion, autotransplants are increasingly used to treat breast cancer, which is now the most common indication for hematopoietic stem cell transplantation. Several factors are identified predicting outcome, enabling doctors and patients to make informed decisions about therapy in particular clinical settings. ABMTR data will be critical for extrapolating results of randomized trials, which tend to be applied in restricted populations, to other patients and in evaluating the impact of preparative regimens, demographic factors, prior treatment and other variables on transplant outcome. The ABMTR provides an important observational database with which to monitor trends and assess new technology.

Dr. Mary M. Horowitz

Autologous Blood and Marrow Transplant Registry (ABMTR),
Health Policy Institute, Medical College of Wisconsin, Milwaukee, WI 53226

References

1. Antman KH, Rowlings PA, Vaughan WP, Pelz CJ, Fay JW, Fields KK, Freytes CO, Gale RP, Hillner BE, Holland HK, Kennedy MJ, Klein JP, Lazarus HM, McCarthy PL, Saez R, Spitzer G, Stadtmauer EA, Williams SF, Wolff S, Sobocinski KA, Armitage JO, Horowitz MM. High-dose chemotherapy with autologous hematopoietic stem cell support for breast cancer in North America. J Clin Oncol 1997;15:1870-9.

2. Rowlings PA, Antman KH, Fay JW, Fields KK, Reed EC, Murphy S, Horowitz MM. Prognostic factors for outcome of autotransplants in women with high risk primary breast cancer. Proceedings of the American Society for Clinical Oncology 1997;16:117a.

3. Rowlings PA, Antman KS, Horowitz MM, Williams SF, Lazarus HM, Fields KK, Pelz CJ, Sobocinski KA, Armitage JO. Prognostic factors in autotransplants for metastatic breast cancer. Blood 1995;86:618a.

4. Rowlings PA, Antman KS, Horowitz MM, Williams SF, Fields KK, Sobocinski KA, Armitage JO for the Breast Cancer Working Committee of the Autologous Blood and Marrow Transplant Registry-North America. Prognostic factors in autotransplants for breast cancer. Proceedings of the American Society of Clinical Oncology 1995;14:325.

5. Williams SF, Rowlings PA. Autologous bone marrow transplant for metastatic breast cancer. Proceedings of the Keystone Symposium, Advances and Controversies in Bone Marrow Transplant, 1995;15(suppl 1):S265-68.
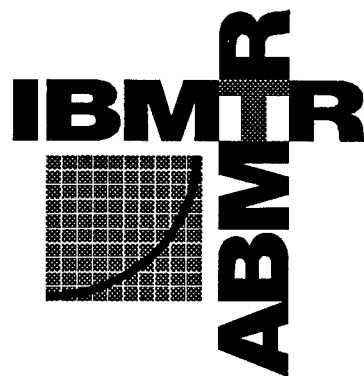
IBMTR/ABMTR Statisticians' Manual
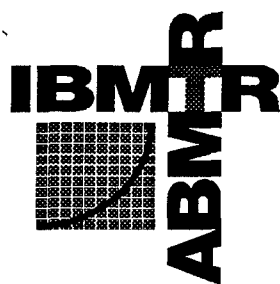
IBMTR/ABMTR Statisticians' Manual

Table of Contents

I. STUDY PROTOCOLS FOR ANALYSES USING IBMTR/ABMTR DATA

The Study Protocol is an invaluable tool for performing analyses of high scientific quality that address important clinical and biologic issues in a way that most efficiently uses the data and personnel resources of the IBMTR and ABMTR. The Study Protocol is also an essential communications tool that clarifies the study objectives of Working/Writing Committee participants and ensures that they will be met by the analyses conducted at the Statistical Center. Ideally, preparation of the Study Protocol will involve as many members of the relevant Committee as possible so that important aspects of the problem under study are addressed to the fullest extent possible. Preparation of the Study Protocol is an important opportunity for Statistical Center personnel to inform Working/Writing Committee participants about the capabilities and limitations of IBMTR/ABMTR data and resources. It also offers Writing/ Working Committee participants to contribute their clinical and scientific expertise. A Study Protocol should be prepared as soon as a Study Proposal (see form in Appendix A) is approved by the relevant Working Committee. The following outline should be used, modified as necessary for the needs of particular projects. A sample Study Protocol is included in Appendix B.

A. OBJECTIVES

The aims of the study should be stated as concisely and clearly as possible. A person reading the Objectives should have clear idea of the primary issue(s) being examined. Examples are: 1. to determine whether allogeneic transplants exert a graft-versus-tumor effect in multiple myeloma; 2. to determine the safety and efficacy of autotransplants for ovarian cancer; or, 3. to compare the efficacy of allogeneic and autologous transplants for acute myelogenous leukemia in first and second remission. Collecting and analyzing data are not objectives in themselves - the objective is the purpose for which the data will be used. Consequently, objectives such as "to collect and analyze data on autotransplants for multiple myeloma" should be avoided.

B. BACKGROUND

This section, generally prepared by the Study Chair, should briefly summarize the rationale for the study, citing relevant previous work. A person reading the Background should have a clear idea of the importance of the intended study. This section gives the statistician performing the study a clearer idea of the clinical and biologic issues involved and identifies studies in the literature which examine similar issues that may provide insight for data analysis. The Background will often be prepared as part of the Study Proposal and may serve as the outline for the Introduction/Discussion of the final manuscript.

C. STUDY POPULATION

The section should clearly define the selection criteria for patients to be included in the analysis. *It should be as specific as possible,* including requirements of age, performance status, disease and disease stage, years of transplant, prior treatment (e.g. persons with CML receiving only hydroxyurea and/or interferon pretransplant), donor type, specific transplant regimens (e.g. methotrexate and cyclosporine for GVHD prophylaxis) or any other restriction relevant to the study. *It is important that these restrictions be defined prospectively based on biologic and statistical principles and not after examination of outcomes.* If the study involves combining IBMTR/ABMTR data with data from another group, the selection criteria for patients in the other database should also be specified (e.g. persons < age 40 years achieving complete remission after induction therapy for AML and receiving high-dose cytarabine for consolidation).

D. OUTCOMES

Outcomes to be studied should be defined clearly, including time-points, where relevant. Outcomes commonly analyzed are discussed in section III of this manual.

E. VARIABLES TO BE ANALYZED

This section is important in that it requires study participants to determine which relevant variables are, in fact, available in the IBMTR/ABMTR database and the format in which the data are collected. All potential outcome and explanatory variables should be listed with suggested categories for analysis. The categories to be used should be discussed with the Study Chair and other Committee members to determine that they are based on sound biological principles and consistent with previous literature. Different studies may require different degrees of detail for specific variables (e.g. conditioning regimen may be considered simply as TBI versus no TBI or as TBI + Cy versus TBI + Cy + VP16 versus Busulfan + Cy versus other specific regimen depending on the objectives of the study). For studies involving combining IBMTR/ABMTR data with data from other groups, the availability of specific variables in both databases should be confirmed. An essential consideration in this regard is the timing of specific measurements. For example, the IBMTR/ABMTR collects data on performance score at the time of transplantation while a chemotherapy database may have available data on performance score at time of diagnosis or remission - since the measurements are at different time points, they cannot be considered equivalent variables. Specifying the list of variables in detail avoids confusion about comparability of data.

If the study requires collecting supplemental data for variables not routinely collected by IBMTR/ABMTR, these variables and plans for supplemental data collection should be specified in this section (see Section IID).

F. METHODS

(1) General approach

This section should describe in non-technical terms the approach to achieving each of the objectives of the study. Data limitations and implications of potential findings may be discussed. For example, to address the objective of determining whether there is a graft-versus-myeloma effect in allografts for multiple myeloma, the general approach might be to compare relapse rates after identical twin transplants and HLA-identical sibling allotransplants for myeloma, adjusting for other factors associated with relapse. A lower relapse rate after allografts would suggest that a graft-versus-myeloma effect exists. The level of detail in this section depends on the issues being addressed and the specifics of the study population.

(2) Statistical methods

This section should include the specific methodology planned, with a discussion of its limitations if relevant. This should include estimations of the power of the analysis to achieve each of the objectives, given anticipated sample size. In contrast to prospective studies, where numbers of patients to be studied is determined by the power desired, IBMTR/ABMTR studies generally focus on a defined number of patients available in the database. The questions that can be answered, therefore, are determined by the numbers of patients available.

G. WRITING COMMITTEE PARTICIPANTS

A Writing Committee must be formed for each study, generally derived from the Working Committee sponsoring the study. Centers contributing large numbers of patients to be included in the study should be contacted to determine whether they wish to have a representative on the Writing Committee, if they have no representative on the Working Committee. If the Study involves collaboration with another Group, the Group should determine the individuals to be included in the Writing Committee. Contact information should be listed for the Study Chair and Co-chairs and the Study Statistician.

H. TIME LINE

A provisional time line for various landmarks in the study should be included. This is especially important when supplemental data must be collected (see section IID). Possible landmarks include: Preliminary analysis of patients to be studied (descriptive characteristics); preparation of supplemental data collection instrument; completion of supplemental data collection; preparation of study file; univariate analyses; multivariate analysis; first draft of manuscript.

II. STUDY FILE PREPARATION

The aim in preparing a study file is to have a study population with selected (by study design) characteristics who are consecutively treated patients at participating centers with adequate follow-up and in large enough numbers to give the analysis sufficient statistical power for its goals. The IBMTR and ABMTR collect data on two levels: *Registration* data and *Research* data. All participating centers *register* consecutive transplants with basic data (age, sex, disease, disease stage and duration, graft type, donor type, conditioning regimen, graft treatment, GVHD prophylaxis and posttransplant disease status, survival, second cancers and primary cause of death). Many centers also also submit detailed data collection forms (Report Forms) with comprehensive clinical and demographic data on a subset of these cases, determined by the Statistical Center and based on needs for current and anticipated studies. Data from Report Forms are entered in the *Research* database. *Registration* data allow analysis of trends in transplant use and outcome and identification of patients for specific studies. Study files, however, generally are generated from the *Research* database.

A) DATA SELECTION

(1) Case Selection

Cases to be analyzed in a specific study will be determined through discussions between the statistician and the Study Chair. As stated in the guidelines for preparing Study Protocols, selection criteria should be defined prospectively based on biologic and statistical principles **not** after the examination of outcomes. The study population is usually limited by disease and type of transplant (either allogeneic or autologous). Other common restrictions include year of transplant, age at transplant, disease stage at transplant, and donor type and tissue type for allogeneic transplants. Restrictions should be applied to the database one at a time with the most important restrictions first and the number of available patients recorded after each restriction is added. Restrictions that result in a study population too small for sufficient statistical power may be liberalized if this would not compromise the scientific goals of the study.

A common problem in case selection is handling cases missing the information used to restrict the population. Whether or not these patients should be excluded should be discussed with the study chair. This results most frequently when the variable is one that has not been collected on all versions of the data collection forms (Report Forms). Discussion should focus on number of cases available for analysis, the number of patients missing the information and the potential biases that may be introduced by excluding these patients. It may be necessary to contact centers reporting these patients to request missing information. Supplemental questionnaires may be designed to capture this information.

(2) Sequential Reporting

IBMTR/ABMTR policy states that all patients who begin their high-dose therapy (conditioning) must be registered with the IBMTR/ABMTR even if for some reason they do not receive their graft. A sequential numbering system (IUBMIDs) must be developed at each center, with each patient numbered consecutively at the time high-dose chemotherapy begins.

While the IBMTR/ABMTR conducts audits annually on randomly selected teams to verify sequential reporting , the statistician should also check for sequential reporting for each center with patients included in the study file. One method to check for sequential reporting is to sort all cases (regardless of disease) by IUBMID. A separate report should be generated for each center. The list of patient identifiers (IUBMID) should be consecutive with no large time intervals between transplant dates. It should be remembered that most but not all teams have separate numbering systems for autologous and allogeneic transplants. Any indication of non-consecutive reporting should be verified by the Communications Coordinator. Centers are required to *register* consecutive patients but are not required to *report* all cases; cases classified (by the Statistical Center) as exempt from reporting are indicated by the variable EXEMPT.

Centers with breaks in sequential reporting should be brought to the attention of the Scientific Director. The center will be contacted and a plan developed to help the team comply with the IBMTR/ABMTR policy of sequential reporting. **All** cases from centers with non-consecutive reporting should be deleted from the analysis, after discussion with the Scientific Director and Study Chair.

(3) Variable selection

Before preparing the study file, the statistician should work closely with the Study Chair to prepare a list of all variables required for analyses which were included in the Study Protocol (see chapter I). Variables will include patient, disease and transplant characteristics and outcome variables (both time intervals and events). The list may be modified after input from the Writing Committee when the Study Protocol is circulated.

For patients with multiple transplants, pretransplant data from the first transplant are generally selected for analyses, while posttransplant data will include both first transplant outcomes and 'global' variables which reflect outcome from all transplants. **In general**, the engraftment, GVHD, infection and posttransplant disease status variables used are those which reflect events after the first transplant, while survival includes the patient's experience through all transplants. The date of second and subsequent transplants should be included in all study files.

B) FOLLOW UP

While most IBMTR/ABMTR analyses use data captured on Report Forms and stored in the *Research* database, the survival, relapse/progression status and dates of relapse/progression and last contact in the research database may not be the most recent available because of delays in follow-up Report submission and entry. Update requests for previously registered cases are distributed approximately every six months and the updated information is added to the *Registration* database. Additionally, survival and disease status information from each follow-up Report Form is added to the *Registration* database as part of the log-in procedure, before the entire Report is keyed into the *Research* database. To use the most recent survival and relapse/progression information on each patient in analyses, last contact data from the *Registration* database must be merged into the *Research* database. The following SAS statements are used to merge two data sets, called *dreg* and *drep*, by TEAM and IUBMID:

PROC SORT DATA=DREG; BY TEAM IUBMID;
PROC SORT DATA=DREP; BY TEAM IUBMID;
DATA MERGED;
MERGE DREG DREP; BY TEAM IUBMID;

Note: The data sets must each be sorted by TEAM and IUBMID before merging.

While the variable names for survival status and survival interval are the same in the *Registration* and *Research* databases, the variables must be renamed in one of the data sets and values compared after merging. (Survivals should never be shorter in the *Registration* database.) A new SAS data set containing the updated survival information can then be created.

IBMTR/ABMTR rules require follow-up through death or 100 days (whichever occurs first) and yearly or at time of death thereafter. Follow-up on patients who die after transplant may be received more quickly than follow-up on patients still alive after transplant. This can lead to survival probabilities appearing worse than they actually are, especially for the more recent years. The purpose of the steps listed below is to ensure that, during the <u>study period selected</u>, patients both alive and dead after transplant have equivalent follow-up. The following steps help identify incomplete reporting:

1. Update patient status using *Registration* data through a chosen date (i.e. patient alive or dead on this day). A patient who dies after the chosen date is considered alive for the current analysis. In general this date should be one year before the study file is prepared to allow adequate time for follow-up to be reported and entered.

2. Create a variable for each patient called TIMEFU for the time between date of last contact and the chosen date. Have the Communications Coordinator request updates on surviving patients with TIMEFU > 12 months.

3. Identify teams, if any, with large proportions of patients with no recent follow-up. These should be contacted in a separate communication (FAX or phone) to determine whether follow-up can be provided in a timely manner for the patients in the study. If not, all patients from these center should be excluded from the study.

4. To identify teams with inconsistencies in the follow-up of dead and living patients the following SAS statements can be used. The median, range and five highest and lowest values and a frequency table for TIMEFU will be printed in the output by team for dead and alive patients:

```
PROC UNIVARIATE FREQ;
VAR TIMEFU;
BY TEAM DEAD;
```

For each team, compare values of variable TIMEFU for dead and alive patients. Since most transplant deaths occur early, TIMEFU should be longer for dead than alive patients. Centers that have, in general, shorter TIMEFUs for dead than living patients may be preferentially reporting deaths. These teams should be investigated further to determine whether this is true and brought to the attention of the Scientific Director. If adequate follow-up on survivors cannot be obtained, all patients in the center should be excluded from analysis.

C) DATA REVIEW

(1) Missing Values

All variables in the study file should be reviewed for missing values before analyses begin. Patients with missing values for key variables may need to be excluded. Missing values result from three causes:

1. Data not requested: data not collected on an older version of a Report Form
2. Data unknown: Center indicates data not known e.g. HSV serology not tested.
3. Data not reported: Item not completed on Report Form.

One way to view the scope of missing data problems, is to create a column titled 'N evaluable' on tables for the Writing Committee. The statistician and Study Chair can review the initial tables and make a plan to address the problem, if necessary. If values for a particular variable are missing for a large percentage of the study population and the variable is not a key one, the variable may be dropped. Alternatively, a related variable which provides similar information may be substituted. In cases where the missing values are critical, the center may be contacted if the missing data falls into categories 1 or 3 above.

(2) Outlier Assessment

Before analyses can begin, data for all patients must be reviewed to determine that all data points appear reasonable. Each dependent and independent variable included in the study file must be checked. Values should fall within expected ranges and all negative values flagged. One way to look for outliers is to use PROC UNIVARIATE in SAS. The following statement will give, along with other information, the median, range, 5% and 95% quantiles, and a stem and leaf plot for DEPVAR1:

```
PROC UNIVARIATE FREQ PLOT;
VAR DEPVAR1;
```

Values above the 95% quantile and below the 5% quantile should be discussed with the Study Chair to determine if the values are appropriate. In some cases, cross tabulations among related variables should be done. The Study Chair can act as a resource in these matters. Report Forms of patients with outliers should be reviewed. In some cases the information may have been entered incorrectly, or the data manager may have made a note in the margin of the Report with an explanation of the value. There may also be attached letters and comments at the end of a Form with further details. When reviewing the Form, also look at the back of the last page to see if the team has been contacted regarding this matter. The team may have already responded to a previous request by the IBMTR/ABMTR regarding the variable. The Communications Coordinator may have recent letters regarding outliers that have not yet been processed and attached to the Report Forms. Finally, it may be necessary to contact the center that completed the Report Form to verify the value in question (see section II.D).

(3) Variables with 'Other' categories

Data collection forms change as technology changes and new drugs and procedures are developed. Some studies may include patients with data collected on older versions of the Report Form. When a drug or procedure is rare, the response to a question may be put into an 'other' category with a space provided to write in the specific information. As the drug comes into frequent use, a new category is created on a new version of the Report Form. At times data in these "other" categories will be needed for analyses. Currently, these data are entered as text field and are retrievable from the database. In the past, only the "other" or a few prespecified categories of "other" were entered. If it is necessary to know what the "other" was, the statistician must work with the Manager of Information Systems to assign personnel to extract and enter this information from the Report Forms.

D) INTERACTION WITH TEAMS

It is sometimes necessary to communicate with Individual centers in preparing a study file. Reasons include:

1. Missing data
2. Data discrepancies/outliers
3. Need for supplemental data not collected on current Report Forms

For discrepancies and missing data, the Communications Coordinator usually contacts the individual center regarding these matters via letter or fax. The following information should be included with each request to facilitate response by the center: registry, Registry ID number, Team number, IUBMID, disease, birth date, and transplant date. For missing data, provide the specific Report Form number, page and item number. For discrepancies and outliers, provide the specific Report Form number, page, item number and the specific question you want answered. If several teams involving many patients must be contacted regarding the same variable, please create worksheets for each center, suitable for faxing, listing the patient information cited above, and space for the team to write in the response. The sheets should be titled with the specific project name and full center name at the top of the page. If a center is responding about multiple patients, the number of patients for each team should be given at the end of each team worksheet. A draft of a letter to the team, to be enclosed with the worksheet, should also be given to the Communications Coordinator. The brief letter should state the project name and purpose of the request, what data are required and the date by which the data are required.

New or more specific data, not collected on the Report Form, is sometimes required for all patients in the study. For a single item, the method described above for obtaining responses for the same variable from multiple teams should be used. Worksheets should be created for every team and a letter drafted, to be included with each worksheet.

Some studies require a supplemental data collection form to be prepared to collect information on new topics involving multiple questions, and dates. The statistician should work closely with the Study Chair and with Manager of Information Systems in designing the new supplemental form. After an initial draft is completed, the draft should be distributed to the rest of the Working Committee for comments and piloted by several data managers to ensure that the responses are as expected. Once the final form is available, it should be given to the Communications Coordinator along with worksheets for every team and a draft of a letter to be included with each worksheet as described above.

E) DATABASE CORRECTIONS

Whenever a team responds with missing data or resolves a discrepancy, the Form must be corrected with red ink, your initials and date noted, and the letter or fax from the team attached to the form. The Report Form is then forwarded to the Systems Coordinator with a note specifying the data base change. (Some changes need physician review before the change is incorporated in the database; this is the responsibility of the Systems Coordinator.)

It may be necessary to also make these changes directly to the study file ('hard code' the changes) if analyses are proceeding quickly. There will be a lag between the time the Systems Coordinator receives the changes and the time an updated database retrieval with the appropriate changes is made.

III. INTERMEDIATE AND TERMINAL EVENTS USED IN STUDIES

A) GENERAL OUTCOMES

(1) Engraftment

Neutrophil Recovery -- defined for separate targets of either ≥ 500 or ≥ 1000 neutrophils/mm^3 as the time to achieve the specific indicator (NEUT5 or NEUT10). The interval variables are INTXNT5 and INTXNT10, respectively, which are measured in days. The interval for a patient who has not achieved the specific indicator is equal to SURVDAYS. This event is summarized by the cumulative distribution function (1-Survival curve).

Platelet Recovery -- defined for separate targets of either $\geq 20,000$, $\geq 50,000$ or $\geq 100,000$ platelets/mm^3 as the time to achieve the specific indicator (PLAT20, PLAT50 or PLAT100). This event is evaluable at 7 days from the last platelet transfusion. The interval variables are INTXP20, INTXP50, INTXP100, respectively, which are measured in days. The interval for a patient who has not achieved the specific indicator is equal to SURVDAYS. This event is summarized by the cumulative distribution function (1-Survival curve).

Graft failure -- Failure to achieve neutrophils ≥ 500/mm^3 or achievement of ≥ 500 neutrophils/mm^3 followed by a decrease to <500/mm^3. The indicator variable is REJECT and the interval variable in INTXFAIL, which is measured in months. The interval for a patient who never achieves neutrophils ≥ 500/mm^3 is 0.03. The interval for a patient who achieves ≥ 500/mm^3 and then has a decrease is the first day the neutrophils are <500/mm^3. The interval for a patient who does not have graft failure (REJECT=0) is equal to INTXSURV. This event is summarized by the cumulative distribution function (1-Survival curve).

(2) Graft-versus-host disease (GVHD)

Acute GVHD -- development of Grade I-IV acute GVHD. The time of first attainment of acute GVHD is the event time even if the maximum grade occurs later. Patients are at risk for this event at 21 days after transplant, if they have evidence of engraftment. In most analyses patients with a grade of II-IV are considered to have acute GVHD and patients with a grade of 0-I are not considered to have acute GVHD. The indicator variable for any Grade II-IV GVHD is AGVHIX1. A variable which indicates both the presence and severity of acute GVHD is AGVH1. The interval variable is DATXAGV1, measured in days. In some studies, particularly those involving donors other than HLA-identical siblings, the incidence of grade III-IV AGVHD is of interest. This indicator variable is AGVHIX34. The interval variable is DATXAG34, measured in days. The interval for a patient who has not achieved the specific acute GVHD indicator is equal to SURVDAYS. This event is summarized by the cumulative distribution function (1-Survival curve).

Chronic GVHD -- development of any chronic GVHD. The time of first attainment of chronic GVHD is the event time. Patients are at risk for this event at 90 days after transplant. The indicator variable for any chronic GVHD is CGVHIX1. The interval variable is INTXCGV1, measured in months. The interval for a patient who has no chronic GVHD is equal to INTXSURV. This event is summarized by the cumulative distribution function (1-Survival curve).

(3) 100 Day Mortality

This event is death prior to 100 days posttransplant. Patients alive at last observation with less than 100 days of follow-up are not considered at risk for this event. The relevant data for this event is a binary variable, MORT100, with the value 1 if they die prior to 100 days and 0 if they are alive at day 100. This event is summarized by the estimated probability of surviving 100 days.

(4) Survival

The variable which indicates which individuals die is SURVHI. The codes 1 and 3 correspond to censored observations. The code 2 corresponds to a death. The time to death (or last contact for survivors) is represented in the variable INTXSURV, measured in months. Patients are at risk for this event at the time of transplant. The event is summarized by a survival curve.

B. LEUKEMIA-SPECIFIC OUTCOMES

(1) Treatment-related Mortality (also called Transplant-related Mortality or Non-relapse Mortality)

This event is defined as death in continuous remission. Patients who relapse or have persistent leukemia are considered censored for this event. The time to the event is coded in the variable INTXRHI, measured in months. For a censored patient without relapse or persistent leukemia, the interval interval is equal to INTXSURV. The variable TXMORT is the event indicator with a code of 1 reflecting death without disease and a code of 0 reflecting a censored observation. Patients are at risk for this event at the time of transplant This event is summarized by the cumulative distribution function (1-Survival curve).

(2) Relapse

This event is defined as a clinical relapse of leukemia. Patients who die without disease are considered censored for this event. The time to the event is coded in the variable INTXRHI, measured in months. For a patient who has not relapsed the interval is equal to INTXSURV. For patients who receive a transplant while not in remission and do not achieve remission the time to the event is set at INTXRHI=0.03 months. The variable REALAPS is the event indicator with a code of 1 reflecting relapse and a code of 0 reflecting a censored observation. Patients are at risk for this event at transplant. This event is summarized by the cumulative distribution function (1-Survival curve).

Some patients, particularly those with chronic myelogenous leukemia, may have recurrence or persistence of a chromosome or molecular marker of their disease without clinical relapse. In most but not all studies, these patients are treated as being in remission until clinical evidence of leukemia develops. A discussion of the definition of relapse with the Study Chair should precede analysis of this variable.

(3) Leukemia -Free Survival (sometimes called Disease Free Survival)

This event corresponds to treatment failure. It is defined as death or relapse. The time to this event is the minimum of the death and relapse time and is coded in the variable INTXRHI, measured in months. For a patient who is alive in remission the interval is equal to INTXSURV. The variable LFS is the event indicator with a code of 1 reflecting death or relapse and a code of 0 reflecting a censored observation. Note that one should check that LFS=TXMORT+REALAPS. Patients are at risk for this event at the time of transplant. The event is summarized by a survival curve.

C. LYMPHOMA AND SOLID TUMOR SPECIFIC OUTCOMES

(1) Treatment Related Mortality

In general the definition is the same as for leukemia, i.e. death in continuous remission. However, lymphoma and solid tumors, even if cured, may take some time to resolve after transplant. Additionally, tests done to evaluate the status of these diseases may not be done for some time after transplant. Consequently a patient may die before the status of the lymphoma or solid tumor is determined. Any death occurring in the first 28 days after transplantation for a lymphoma or solid tumor is considered to be treatment related. Deaths occurring in the next 72 days are assumed to be treatment-related if the disease status is reported as unknown or not evaluable. The latter cases should be reviewed by the Study Chair. The indicator variable is TXMORTL with a value of 0 for censored cases and a value of 1 for patients reflecting treatment-related mortality. The interval variable is INTXREL, which is the time to relapse or death in remission, measured in months. For patients who are censored alive, INTXREL is equal to INTXSURV.

(2) Progression

This event is defined as an increase in the size of sites of known disease or development of new sites of disease after transplant. It may follow a period of "stable" disease where the lymphoma or solid tumor has < 50% reduction in known sites of disease but not new sites of disease and no increase of disease at any site. It may follow a partial remission where the tumor had a 50-99% reduction in size with no new sites of disease. It may follow a complete remission. Any recurrence of tumor or increase in size of tumor after a complete or partial remission is considered progression, even if the extent of tumor is less than pretransplant. Patients who die without progression (may have stable disease, partial or complete remission) are considered censored for this event. The time to the event is coded in the variable INTXPROG, measured in months. For censored patients the variable INTXPROG is equal to INTXSURV. The variable PROGRESS is the indicator of progression with a value of 1 reflecting progression and a value of 0 denoting a censored observation. Patients are at risk of this event 28 days after transplant. This event is summarized by the cumulative distribution function (1-survival).

(3) Progression- Free Survival

This event is defined as death or progression. The time to this event is the minimum of the death and the progression times. The time to the event is coded in the variable INTXPROG, measured in months. For patients who have not progressed, INTXPROG is equal to INTXSURV. The variable PFS is the event indicator with a value of 1 reflecting death in the first 28 days posttransplant or death or progression after day 28 posttransplant. A code of 0 denotes a censored observation. Patients are at risk for this event at the time of transplant. This event is summarized by a survival curve.

(4) Relapse (Or Recurrence)

This event is defined as clinical recurrence of disease after a posttransplant remission. *For patients transplanted in remission or for patients who achieve a complete remission after transplant,* recurrence is the same as progression. The interval is coded in the variable INTXREL, measured in months. The variable RECUR is the indicator of recurrence with a code of 1 reflecting relapse and a code of 0 reflecting a censored observation. Patients transplanted in remission or who achieve remission after transplant are at risk after 28 days posttransplant for this event. This event is summarized by the cumulative distribution function (1-Survival curve).

(5) Disease-Free Survival

The event is defined as death or recurrent disease. The time to this event is the minimum of the death and relapse times, where patients who never have a complete remission posttransplant are considered to experience the event at day 1. The time is coded in the variable INTXREL, measured in months. The variable DFS is the event indicator with a code of 1 reflecting the event has occurred and a code of 0 reflecting a censored observation. The event is summarized by a survival curve.

TABLE OF VARIABLE NAMES

Variable	Indicator (values)	Interval From Transplant (units)
Engraftment		
500 neutrophils/mm³*	NEUT5 (0,1)	INTXNT5 (days)
1000 neutrophils/mm³*	NEUT10 (0,1)	INTXNT10 (days)
20,000 platelets/mm³*	PLAT20 (0,1)	INTXP20 (days)
50,000 platelets/mm³*	PLAT50 (0,1)	INTXP50 (days)
100,000 platelets/mm³*	PLAT100 (0,1)	INTXP100 (days)
Graft Failure	REJECT (0,1)	INTXFAIL (months)
GVHD		
Acute GVHD grade 0-4	AGVH1 (0,1,2,3,4)	DATXAGV1 (days) or INTXAGV1 (months)
grade 0,1 vs 2,3,4	AGVHIX1 (0,1)	DATXAGV1 (days) or INTXAGV1 (months)
grade 0,1,2 vs 3,4*	AGVHIX34 (0,1)	DATXAG34 (days) or INTXAG34 (months)
Chronic GVHD grade 0,1,2,4	CGVH1 (0,1,2,4)	DATXCGV1 (days) or INTXCGV1 (months)
grade 0 vs 1,2,4	CGVHIX1 (0,1)	DATXCGV1 (days) or INTXCGV1 (months)
100 Day Mortality		
100 day mortality*	MORT100 (0,1)	
Survival		
Vital Status	SURVHI (1,2,3)	INTXSURV (months)
Leukemia-Specific Outcomes		
Treatment-related mortality	TXMORT (0,1)	INTXRHI (months)
Relapse	REALAPS (0,1)	INTXRHI (months)
Leukemia-free mortality	LFS (0,1)	INTXRHI (months)
Lymphoma and Solid Tumor Specific Outcomes		
Treatment-related mortality*	TXMORTL (0,1)	INTXREL (months)
Progression*	PROGRESS (0,1)	INTXPROG (months)
Relapse/Recurrence*	RECUR (0,1)	INTXREL (months)
Disease-free survival*	DFS (0,1)	INTXREL (months)

* Variable is NOT currently coded in retrieval; must be computed in study file

IV. DESCRIPTIVE STATISTICS

Descriptive statistics are used to summarize the characteristics of a data set. They are used to check for outliers, to test for differences in the study population when a hypothesis testing model is to be built and to help in discretizing continuous covariates for use in future analyses.

A) DISCRETE COVARIATES

For the discrete covariates, we calculate the number and percentage of patients for each category. In a hypotheses testing study the chi-square test is used to check whether the covariate has same distribution for all levels of the main effect.

Summary statistics and tests are performed using the SAS procedure FREQ. For example, the following SAS procedure will yield the number and percentage of males and females for each treatment group, and *p-value* of the chi-square test:

PROC FREQ; TABLES SEX*GROUP / CHISQ;

When the sample size is small relative to the size of a contingency table, chi-square test may not be a valid test. In this case SAS will print a warning message that the chi square test is not valid. In such a case, Fisher's exact test is a more appropriate test. We then change "chisq" option to the option "exact" in the SAS code which will give us the *p-value* of Fisher's exact test.

B) CONTINUOUS COVARIATES

For continuous covariates we report, in writing committee memos or maunuscripts, medians and ranges for the variable. For discussion at statistical staff meetings or with the clinical investigator, we use the SAS procedure PROC UNIVARIATE to compute summary statistics that allow us to check for outliers. The coding for this procedure for a covariate age is

PROC UNIVARIATE PLOT FREQ; VAR AGE;

This command will produce summary statistics (mean, median, range, standard deviation, etc.), a stem-and-leaf plot or a histogram, and the estimated frequencies for each value of the variable. To identify outliers one could add the statement ID PATIENTNO; , for example, where PATIENTNO is some identifier of the patient. This will associate the value of PATIENTNO with the values UNIVARIATE prints for the five largest and smallest observations. Using a BY variable, one can have SAS produce a UNIVARIATE analysis for each level of the factor of primary interest in a hypothesis testing study.

When the goal of the study is to compare outcomes between treatment groups, the Kruskal-Wallis test is used to check if the distribution of a continuous factor is the same over the groups. The SAS procedure used is PROC NPAR1WAY which is coded as follows:

PROC NPAR1WAY WILCOXON; CLASS GROUP; VAR AGE;

C) FOLLOW-UP TIME

To compare the survival probabilities, we need to study the follow-up time. We use the product-limit estimator proposed by Kaplan-Meier to estimate the probability of the follow-up time, and log-rank test to test if the cohorts have same probability of follow-up times. To do so, let TIME be the time of event or end of follow-up, and STATUS be the indicator of censorship; that is STATUS=1 if patient is still alive; 0 otherwise. Note that here we are coding deaths as censored observations and usual censored observations as events since we are trying to estimate the distribution of the on study times if patients had not died.

The SAS procedure LIFETEST will estimate the probability distribution of the follow-up time, the median follow-up time, the range of follow-up times (largest and smallest on study times) and *p-value* of the log-rank test which is used to check for differences between groups:

PROC LIFETEST; TIME TIME*STATUS(0); STRATA GROUP;

D) SURVIVAL

The survival curves are useful for preliminary examination of the data, for computing the common interested quantities such as median survival time or the probability of survival at some point in time, and for evaluating the fit of regression models. The standard tests for comparing survival curves across the different treatment groups are important for analyzing the data. In survival analyses the time to event data could be censored and/or truncated. Here we only discuss the methods involving right censored time to event data. For other type censored or truncated data see Klein and Moeschberger (1997).

(1) Summary Curves

The standard estimator of the survival curve is the product-limit estimator which was proposed by Kaplan-Meier (1958), and is often called the Kaplan-Meier estimator or the actuarial estimate. The variance of the product-limit estimator is estimated by Greenwood's formula. The SAS's PROC LIFETEST procedure provides this estimates of survival functions and it's standard error. Let TIME be the event time and STATUS be indicator of the noncensorship, that is, STATUS=1 if event occurred and 0 otherwise. The SAS codes are

```
PROC LIFETEST;
TIME TIME*STATUS(0);
```

This command will produce the summary survival curve. To make plots of the survival curves an output data set can be produced which contains the survival estimates and their standard errors. An example of the coding is as follows:

```
PROC LIFETEST DATA=TEMP NOPRINT
OUTSURV=PLOTME;
TIME INTXRHI*NLFS(0);
STRATA DISPX;
```

This coding produces the data set TEMP which contains the following variables:

DISPX -- The stratification variable
INTXRHI --The time variable
CENSOR -- The indicator of censoring (1-censored, 0-dead)
SURVIVAL --The estimate of the survival function at time INTXRHI in strata
         DISPX
SDF_LCL   SDF_UCL -- 95% Naive confidence interval for the survival function
STRTUM -- Strata number

Note that for a censored observation the values for the confidence interval are missing.

To plot the survival curves the following code could be used. In this case there are 5 levels to the variable DISPX. We will create variables S1, ..., S5 which have the estimates for the respective strata. (In the data statement the variables R1, ..., R5 are the estimates of 1-SURVIVAL used when drawing graphs for relapse curves). To Indicate a censored observation we will put the symbol "I" at each censored observation. The values of the survival function at the

censored observation are coded in CS1, ..., CS5 (CR1, ... , CR5 for relapse). The data set revised is used in plotting.

```
DATA REVISED; SET PLOTME;
IF _STRTUM_=1 THEN DO;
   S1=SURVIVAL;
   R1=1-SURVIVAL;
   IF _CENSOR_ = 0 THEN CS1=.;
   ELSE DO; CS1=S1;  CR1=R1; END;
   END;
ELSE IF _STRTUM_=2 THEN DO;
   S2=SURVIVAL;
   R2=1-SURVIVAL;
   IF _CENSOR_ = 0 THEN CS2=.;
   ELSE DO; CS2=S2;  CR2=R2; END;
   END;
ELSE IF _STRTUM_=3 THEN DO;
   S3=SURVIVAL;
   R3=1-SURVIVAL;
   IF _CENSOR_ = 0 THEN CS3=.;
   ELSE DO; CS3=S3;  CR3=R3; END;
   END;
ELSE IF _STRTUM_=4 THEN DO;
   S4=SURVIVAL;
   R4=1-SURVIVAL;
   IF _CENSOR_ = 0 THEN CS4=.;
   ELSE DO; CS4=S4;  CR4=R4; END;
   END;
ELSE IF _STRTUM_=5 THEN DO;
   S5=SURVIVAL;
   R5=1-SURVIVAL;
   IF _CENSOR_ = 0 THEN CS5=.;
   ELSE DO; CS5=S5;  CR5=R5; END;
   END;
```

PROC GPLOT is used to draw the graph. We are plotting 10 curves so 10 SYMBOL statements are needed. For the first 5 a step function is drawn. These are the curves S1,. .., S5. For the next 5, no curve is drawn. Only the symbol l is plotted.

```
PROC GPLOT DATA=REVISED;
SYMBOL1 REPEAT=5 COLOR=BLACK I=STEPLJ V=NONE W=1 L=1;
SYMBOL2 R=5 COLOR=BLACK I=NONE F=SWISS  V='l';
PLOT (S1 S2 S3 S4 S5 CS1 CS2 CS3 CS4 CS5)*INTXRHI/OVERLAY;
RUN;
```

(2) Comparisons of Survival Curves

If two different treatments are given to two groups separately, one of the most important questions would be "Did two treatments make a difference in the probability of survival?". To answer this question, we need to test the null hypothesis that the survival functions are same across the two treatment groups, that is $H_o: S_1(t)= S_2(t)$, for all t, where $S_1(t)$ and $S_2(t)$ are the survival functions for treatment group 1 and 2 separately. We use a log-rank test for testing this null hypothesis (see Klein and Moeschberger Section 7.3). The SAS codes for the log-rank test are

```
PROC LIFETEST;
TIME TIME*STATUS(0);
STRATA GROUP;
```

Note that the "TEST" statement in PROC LIFETEST is **not** used here.

The above test is a comparison of the entire survival curves. Occasionally we wish to compare two curves at a fixed point in time, T_0. To perform this test the following statistic is used

$$Z = \frac{S_1(T_0) - S_2(T_2)}{\sqrt{V[S_1(T_0)] + V[S_1(T_0)]}} ,$$

where $V[S_k(T_0)]$ is the estimated variance of the Kaplan-Meier Estimator for group k, k=1,2. This test is typically done by hand on a calculator using the output of PROC LIFETEST.

(3) Confidence Intervals for Survival function

As noted above the output data set from PROC LIFETEST contains a 95% confidence interval for the survival function. Recent statistical literature suggests that these intervals are suspect for small to moderate samples. A better way of constructing intervals is to use the log transformed intervals (Klein and Moeschberger Section 4.3). The formula for these intervals is as follows

$$(S(t)^{1/\theta}, S(t)^{\theta}) \text{ where } \theta = \exp\{\frac{Z_{1-\alpha/2}\,\sigma(t)}{\ln[S(t)]}\}, \text{ and } \sigma^2(t) = V[S(t)]/S(t)^2.$$

Using the output data set from LIFETEST a 95% confidence interval can be computed as follows:

```
DATA NEW; SET OLD;
SE=(SDF_UCL- SDF_LCL)/(2*1.96*SURVIVAL);
THETA=EXP(1.96*SE/LOG(SURVIVAL));
LOWER=SURVIVAL**(1/THETA);
UPPER=SURVIVAL**THETA;
```

Note that the confidence intervals constructed in this manner are pointwise intervals.

E) 100 Day mortality

When analyzing bone marrow transplant data it is sometimes important to study 100 day mortality. In the research database, virtually all patients either died within 100 days or had follow-up time longer than 100 days since 100 days of follow-up is required for the initial report form. In the registration database, there are some cases with follow-up time less than 100 days. However, the percentage of such cases is very small (less than 1%). For those patients with follow-up times less than 100 day,s whether they will die within 100 days is unknown. We exclude these cases when analyzing the 100 day mortality rate. We use a chi-square test to test whether the 100 day mortality rates are same across the treatment groups. Define the variable Z=1 if patients died within 100 days and 0 otherwise. The SAS codes are

```
PROC FREQ; TABLES Z*GROUP / CHISQ;
```

V MULTIVARIATE MODELS FOR SURVIVAL

In this section we discuss statistical procedures for modeling multivariate survival. Mutivariate survival modeling is used in two related situations: The first is the situation where we wish to compare two or more groups after making adjustments for other factors which may influence outcome. The second is where we wish to determine which risk factors may be related to a given outcome. We shall term these hypothesis testing and exploratory model building analyses, respectively.

A. Definitions

Factors

The analysis to be performed is a regression analysis where the endpoint is the time to some event (See Section III for a definition of the event times). The time to event is called the dependent variable. Explanatory information is contained in a set of *factors*. A factor is a set of explanatory covariates that describes a particular attribute of the patient being transplanted. Associated with a factor is a degree of freedom. The *degree of freedom* is the number of independent variables which make up the factor.

When the phenomena under consideration is categorical with k categories, then the factor consists of k-1 binary covariates with each indicating a given level of the covariate (one level is the baseline so only k-1 levels are needed). It should be noted that the coding within a factor is not unique, since any one of the k levels can be used as the baseline. However, when making an inference about a factor any of the equivalent codings will give rise to the same conclusion.

As an example consider the coding of a factor which represents the sex of the donor and recipient of an Allo transplant. This factor will have three degrees of freedom and require the definition of three binary covariates. One coding, which has the male donor and male recipient (M->M) as the baseline is:

$$Z_1 = \begin{cases} 1 \text{ if F-> F} \\ 0 \text{ otherwise} \end{cases}$$

$$Z_2 = \begin{cases} 1 \text{ if F-> M} \\ 0 \text{ otherwise} \end{cases}$$

$$Z_3 = \begin{cases} 1 \text{ if M-> F} \\ 0 \text{ otherwise} \end{cases}$$

An alternate coding (with the same baseline is)

$$Z_1 = \begin{cases} 1 \text{ if Female donor} \\ 0 \text{ otherwise} \end{cases}$$

$$Z_2 = \begin{cases} 1 \text{ if Female recipient} \\ 0 \text{ otherwise} \end{cases}$$

$$Z_3 = \begin{cases} 1 \text{ if Female Donor and Recipient} \\ 0 \text{ otherwise} \end{cases}$$

Other examples of factors are as follows:

Factor	Coding	Degrees of Freedom
Age as a continuous factor	$Z = Age$	1
Age Categorized into 0-10[1],10-20,>20	$Z_1 = \begin{cases} 1 \text{ if } 10<Age\leq20 \\ 0 \text{ otherwise} \end{cases}$ $Z_2 = \begin{cases} 1 \text{ if } Age>20 \\ 0 \text{ otherwise} \end{cases}$	2
Year of Transplant[2] (Patients transplanted in 87-92)	$Z_1 = \begin{cases} 1 \text{ if } 88 \\ 0 \text{ otherwise} \end{cases}$ $Z_2 = \begin{cases} 1 \text{ if } 89 \\ 0 \text{ otherwise} \end{cases}$ $Z_3 = \begin{cases} 1 \text{ if } 90 \\ 0 \text{ otherwise} \end{cases}$ $Z_4 = \begin{cases} 1 \text{ if } 91 \\ 0 \text{ otherwise} \end{cases}$ $Z_5 = \begin{cases} 1 \text{ if } 92 \\ 0 \text{ otherwise} \end{cases}$	5

1) 0-10 baseline
2) 87 Baseline

Factors can be either *fixed time* or *time dependent* factors. A fixed time factor is one whose value is know at the time of transplant (or at the "zero" time of the study). Examples of fixed time factors are year of transplant, preparative regimen, age, sex, GVHD prophyaxis, etc. Fixed time covariates are dealt with in Chapter 8 of Klein and Moeschberger

Time dependent factors are those whose values are not known at the time of transplant. These may be measurements taken at some planned point after transplant, (e.g. Karnofsky score at 6 months post transplant), the occurrence of intermediate events (e.g., occurrence of acute GVHD, platelet recovery time, etc.), events which happen at some time after transplant (e.g. second transplant), or artificially created (e.g., factors used to check model assumptions or factors to adjust for non proportional hazards (See V.C below)).

Censoring and Truncation

Right censoring occurs when at the last observation of the subject the event under study has not yet occurred. This may be because either the patient is still alive and disease free at their last observation time, because the patient was lost to follow-up, or because some other event not under study occurred. Censored data is partial information about the timing of the event of interest in that all we know is that for this patient the event has yet to occur at the last time we saw the patient. The following table summarizes censoring for some common events we study.

Event of Interest	Patient Status at last follow-up which leads to censoring
Death	Alive
Relapse or Progression	Alive and Disease free Dead without Disease
Treatment related mortality	Alive and Disease Free
Acute GVHD	Dead without acute GVHD Alive without acute GVHD
Chronic GVHD	Dead without chronic GVHD Alive without chronicGVHD

Left Truncation occurs when some intermediate event must occur before the patient becomes at risk to experience the event in which we are interested. That is when the event time, X, is measured from some landmark but only subjects who experience some intermediate event at time, V, are to be included in the study. This is the case, for example if we wish to draw inference about X, the time from transplant to death or relapse, for those patients whose platelets have recovered to a self sustaining level. If V is the time until platelets recover for the patient, then only patients who experience this intermediate event are entered into the study. Life lengths in this study will be left truncated. The times V are sometimes called *delayed entry times..*

Left truncation also occurs when we are comparing patients given a transplant to those given chemotherapy. Since we only observe patients who were transplanted in our data base, if the "zero" point is the time of diagnosis, then our patients are not a risk to die until they are transplanted and as such they are left truncated at the time of transplant. Section 9.4 of Klein and Moeschberger discuss left truncation.

Cox Regression Model and Relative Risks

The basic model for analysis is the proportional hazards model or the Cox regression model. For this model the hazard rate for an individual with set of covariates $(Z_1(t), ..., Z_p(t))$ is

$$h[t \mid Z_1(t), ..., Z_p(t)] = h_0(t) \exp[\beta_1 Z_1(t) + ... + \beta_p Z_p(t)].$$

Here the β's are called *risk coefficients* and $h_0(t)$ is the arbitrary *baseline hazard rate.* Estimation of the risk coefficients for this model is based on a *partial likelihood function.* While there are several formulations for this partial likelihood we shall use the default partial likelihood available in SAS[@], namely *Breslow's* partial likelihood. (See Klein and Moeschberger Section 8.3).

Estimates of the β's, denoted by $b_1, ..., b_p$, and the covariance matrix of the estimates are available in the SAS[@] procedure PHREG.

When all the factors are fixed then the *relative risk* of the event for a patient with a set of covariates, $Z_1, ..., Z_p$ as compared to a patient with covariates $Z_1^*, ..., Z_p^*$ is the ratio of their respected hazard rates, which in this model is given by

$$\exp[\beta_1 (Z_1 - Z_1^*) + ... + \beta_p (Z_p - Z_p^*)]. \tag{1}$$

When Z_k are binary covariates (i.e. 0 1 valued) the quantity $\exp[\beta_k]$ is often called the relative risk of the covariate Z_k. Here this quantity is the ratio of the hazard rate of someone with a value of 1 for this covariate as compared to someone with a value of zero for this covariate, when all other covariates are the same for the two individuals. When Z_k is one of the covariates that make up a factor then this is the relative risk of an individual with category Z_k compared to a baseline individual, again all other factors held the same. Relative risk of an individual with category k as compared to an individual with category j of a given factor is given by $\exp[\beta_k - \beta_j]$, which is a special case of (1).

$100 \times (1-\alpha)$ confidence intervals for the relative risk are given by the following formula:

Estimate $= \exp[b_k]$
Confidence Interval $= (\exp\{b_k - z_{1-\alpha/2} SE[b_k]\}, \exp\{b_k + z_{1-\alpha/2} SE[b_k]\})$

Estimate $= \exp[\beta_1 (Z_1 - Z_1^*) + \ldots + \beta_p (Z_p - Z_p^*)]$

Confidence Interval $=$

$(\exp\{b_1 (Z_1 - Z_1^*) + \ldots + b_p (Z_p - Z_p^*) - z_{1-\alpha/2} S\}, \exp\{b_1 (Z_1 - Z_1^*) + \ldots + b_p (Z_p - Z_p^*) - z_{1-\alpha/2} S\}),$

where

$$S^2 = \sum_{j=1}^{p} Var[b_j](Z_j - Z_j^*)^2 + \sum_{i \neq j} Cov[b_j, b_i](Z_j - Z_j^*)(Z_i - Z_i^*)$$

and $Z_{1-\alpha/2}$ is the $(1-\alpha/2)$ percentile of a standard normal.

B. Creating Factors For Dependent Variables

1. Categorical Data

If the variable has k categories then k-1 binary covariates are created. Each covariate is the indicator of whether a patient is in a particular category. One category is the baseline and when a patient is in this category all of the k-1 covariates are zero.

Each category must contain at least 5% of the sample and at least 5% of the events to be considered as a separate category. If this criterion is not met then the category must be collapsed with another biologically compatible category or cases with this category should be excluded from the study.

2. Missing values

When the number of missing values is small or the number of events with missing data is small then these cases are excluded from the study. By a small number of cases we mean less than 5% of the data or less than 20, which ever number is smaller. By a small number of events we mean less than 5% of the events or 5 events, which ever is smaller.

When the number of missing values is large then missing is considered as a separate factor and the number of categories is increased by 1.

These determinations should be made before any attempt at modeling the factors related to the event time is performed and before any diagnostic checks are made.

3. Discretizing a continuous covariate

Categorical covariates are easier to interpret and should be used in most cases. To determine the cut points to use the following procedure is used.

Step 1. Use biologically relevant cut points. These cut points are based on the physician investigators knowledge of the biology of the disease and transplant regime under study. They may be based on the transplant literature, consensus of the Writing or Working committee, or based on accepted practice in previous IBMTR/ABMTR studies. These cut points should be listed and discussed in the study protocol. Some categories for common covariates for all disease are listed in the following table:

Factor	Categories
Karnofsky Score Pre Transplant	<90, ≥90
Patient Age	By Decade (0-9, 10-19,...,40-50,>50)
Donor Age	By Decade (0-9, 10-19,...,40-50,>50)
Year of Transplant	80-85, 86-90, >90
WBC count at Diagnosis	$< \text{vrs} \geq 75 \times 10^9/\text{L}$

Some disease specific factorsspecific to studies of lukemia are as follows:

Time to achieve first remission	$< \text{vrs} \geq 8$ weeks
Duration of first remission	$< \text{vrs} \geq 8$ weeks
Interval between transplant and most recent remission	$< \text{vrs} > 1$ year
WBC at Diagnosis	AML: $< \text{vrs} \geq 75 \times 10^9/\text{L}$ ALL (adults): $< \text{vrs} \geq 30 \times 10^9/\text{L}$ ALL (Children): $< \text{vrs} \geq 100 \times 10^9/\text{L}$ CML : $< \text{vrs} \geq 20 \times 10^9/\text{L}$

Step 2. When cut points can not be agreed to in step one then a statistical method is used to find the cut point. A set of possible cut points is made. In theory the cut point to discretize a continuous covariate can at any value in the data set that corresponds to an event, the set of cut points will be restricted to "nice" values, typically integers or some multiple of the integers (e.g.. for ages 5, 10,15, 20, etc. years). Separate proportional hazards models are fit which includes only the single factor for each plausible discretation of the covariate. The partial log likelihood is recorded for each of these models (or the -2xlog likelihood value). The categorization which gives the largest of these partial likelihoods is then used in subsequent analyses. Note that in this technique the number of categories must be predetermined and each of the likelihoods is for a factor with the same degrees of freedom.

NOTE: The proposed categories for all continuous covariates must be circulated to the Writing Committee for review before any multivariate analysis is performed.

3. Creating Time Dependent Covariates

There are two types of time dependent covariates, internal and external covariates. Internal covariates are intrinsic to the transplant process (e.g. acute GVHD) and external covariates are artificially created covariates typically arising by the need to either check the proportionality assumption or to adjust fixed covariates for non-proportional hazards. The creation of external covariates is discussed in Section V.C.

An internal covariate for an intermediate event is coded as follows:

$$Z(t) = \begin{cases} 1 \text{ if time to intermediate event} \leq t \\ 0 \text{ otherwise} \end{cases}$$

In PROC PHREG we could code acute GVHD as follows:

```
PROC PHREG;
MODEL TSUR*DEAD(0)=AGVH;
IF TAGVH <=TSUR AND IAGVH=1 THEN AGVH=1; ELSE AGVH=0;
```

Here TSUR is the time to the event; DEAD the event indicator with 0 indicating a censored observation; TAGVH the time to acute GVHD and IAGVH the indicator of acute GVHD with 1 denoting that acute GVHD has occurred.

Caveat emporia: When a time dependent covariate for an intermediate event is used only patients at risk for the event should be in the data set. For example to study acute GVHD only patients who have survived at least 21 days are included in the study. See Section III for these inclusion criterion.

C. Checking Model Assumptions

1. Testing for proportional hazards

To check the assumption of proportional hazards an external time dependent covariate approach is used. Here a time dependent covariate is created for each of the covariates which make up a given factor. The covariate is of the form $Z(t) = Z \ln(t)$. A model is fit with both the orginal fixed time covariates and the created time dependent covariates. If the factor has k degrees of freedom then a Wald test, with k degrees of freedom, is performed to test that the hypotheses all the risk coefficients associated with the time dependent covariates are equal to zero. If this hypothesis is rejected than the factor has non proportional hazards. A 5% signficance level is used for this test.

The testing for proportional hazards is performed separately for each factor. When the goal of the analysis is to test a particular hypothesis then the main factor of interest is included in each model.

The SAS@ code to perform this analyses for a 3 degree of freedom factor with covariates Z1, Z2, Z3, a time to event TSUR and and event indicator DEAD (with code 0 for censored observations) is as follows:

```
PROC PHREG;
MODEL TSUR*DEAD(0)=Z1 Z2 Z3 ZP1 ZP2 ZP3;
PROP: TEST ZP1=ZP2=ZP3=0;
ZP1=Z1*LOG(TSUR);
ZP2=Z2*LOG(TSUR);
ZP3=Z3*LOG(TSUR);
```

B ADJUSTMENTS FOR NON PROPORTIONAL HAZARDS

When the proportional hazards assumption is rejected than an adjustment to the model is needed. The adjustment depends on the number of non proportional hazards found, and whether estimates or tests of the effect of the factor with non proportional hazards is of interest.

If there are few factors, the factors are not of primary interest in the study and these factors have few categories then the analyses should be based on a stratified model. Here a single variable is created which includes a distinct value (the actual values of the variable are irrelevant) for each level of the factor. The model is then stratified on these new variables. In the above example the following SAS@ code would be used to test a hypotheses about a new covariate, MAIN, stratifying on the factor Z1, Z2, Z3.

```
DATA NEW; SET OLD;
STRAT=0;
IF Z1=1 THEN ST=1;
IF Z2=2 THEN ST=2;
IF Z3=3 THEN ST=3;
PROC PHREG;
MODEL TSUR*DEAD(0)=MAIN;
STRATA ST;
```

A rule of thumb for determining if stratification is to be used is that each stratum should contain at least 20 observations and at least 5 events.

When stratification is not warranted then an artificial time dependent covariate is created to handle the non proportional hazards. That is we create two time dependent covariates for a given non-proportional hazards covariate. These are the early ($t \leq \tau$) and late ($t > \tau$) effects of covariate represented by the covariates

$$ZE(t) = \begin{cases} Z & \text{if } t \leq \tau \\ 0 & \text{otherwise} \end{cases} \qquad ZL(t) = \begin{cases} Z & \text{if } t > \tau \\ 0 & \text{otherwise} \end{cases}.$$

To find τ the approach for finding the best cut point for a continuous covariate is used (See Section V.B.3.). In theory the only values one needs to check are the observed event times but in practice one should attempt to pick a set of biologically plausible values τ and check the likelihood at these points. Once τ is found then the proportional hazards assumption must be checked for each of the newly created time dependent covariates. If the assumption is found not to be valid then the above process is repeated.

D. Stepwise Model Building

1 Initial Search

Stepwise model building is done either in hypothesis testing or exploratory analysis problems. The difference between the two is in the hypothesis testing situation the main effect to be tested is included in all models. The procedure is only used after the factors have been checked for proportional hazards and all problems with missing values have been resolved by either cleaning the data set or by creation of a missing category. The data set for this procedure must be the same for each of the models to be run for the procedure to be valid. The automated procedures in SAS$^{@}$ can only be used when all factors are single degree of freedom factors.

If there are M factors (other than the main effect) to be considered then the model building is as follows:

Step 1: Fit M models with each model containing only a single factor. Find the Wald p-value associated with the test of no effect of this factor on outcome. The factor with the smallest p-value (<0.05) is put into the model. Note if none of the factors are signficant at the 5% level then the final model has no factors in it (except for the main effect in the hypothesis testing framework).

Step J, J=2,...,M:

A. Fit M-(J-1) models with the J-1 factors left in the model from step J-1 along with one of the M-J+1 factors not in the model at the previous step included in the model. Find the Wald p-value for each new factor.

B. If none of the new factors are signficant at the 5% level (i.e. all have a p-value >0.05) then stop and used the model from step J-1.

C. If one of the factors has a p-value less than 0.05 then add it to the model and got to step J+1.

The model from this procedure is the working model. If all factors (except the possible main effect) are significant then it is the stage one model. If there is some factor, added at an earlier step, which is no longer significant then further tests should be performed on the model to remove non significant factors. In most cases this means that two of the factors are highly associated and the covariate which is simplest to interpret should be included in the final model. Finding the final model in this case will involve comparing models with and without the factor. Note models can be compared on the basis of the Akaike Information Criterion, AIC = -2 Log L + 2p, where p is the number of regression parameters in the model and L is the partial log likelihood.

2. Collapsing Categories

Once a first stage model is found it is reasonable to examine, in this model, the potential of collapsing categories for the individual factors. This should be done in collaboration with the physician investigator on the project so that biologically implausible categories are not created. If there are k categories there are $kx(k-1)/2$ tests to be performed. The tests are comparisons of each category with each other. For example if there are four categories, coded by three binary covariates Z1, Z2, and Z3, then the $4x3/2=6$ tests are as follows:

H_0 $\beta1=1$ (category 1 = baseline)

H_0 $\beta2=1$ (category 2 = baseline)

H_0 $\beta3=1$ (category 3 = baseline)

H_0 $\beta1=\beta2$ (category 1 = category 2)

H_0 $\beta1=\beta3$ (category 1 = category 3)

H_0 $\beta2=\beta3$ (category 2 = category 3).

Based on these tests the decision to recategorize the factor can be made and a phase two model with revised factors can be constructed. Of course the factors need to be retested in this revised model.

3. Testing for interactions

Interactions are tested in the phase two model. Which interactions to check should be a collaborative decision between the physician investigator and the statistician. In general it is advisable to check for interactions between a main effect and each of the factors being used to adjust for differences in the treatment arms.

To check for an interaction of a factor with M levels and a factor with P levels requires the creation of MxP-1 binary covariates. To test for interaction we create (M-1)x(P-1) new covariates by multiplying each of the (M-1) binary covariates of factor 1 by one of the (P-1) covariates of factor 2. A model is fit with the main effects of factors 1 and 2 (M+P-2 covariates) and the (M-1)x(P-1) new covariates (and any other factors in the phase two model). A Wald test, with (M-1)x(P-1) is performed to test the hypothesis that the interaction covariates are all zero. If this test has a p-value greater than 0.05 the an interaction is not present.

If an interaction is found between two factors then the two factors are pooled into a single factor with (MxP) categories (MxP-1 binary covariates) found by picking one category from factor 1 and one from factor 2. Using the technique in Section V.D.2 the dimensionally of this factor is reduced to achieve a new model.

E Testing for center effects

To test for possible center effects a random effects score test developed by Commange and Andersen (1995) is used (See Klein and Moeschberger Section 13.2). The test is performed on the final model for the study and tests the hypothesis that there is no center effect against the hypothesis of a random center effect. A FORTRAN program is available to perform the test. Input to the program is the estimates of the risk coefficients from the final model, the estimated covariance matrix of the risk coefficients and the raw data.

If the score test rejects the hypothesis of no center effect then an adjustment for this effect is made using a Gamma frailty model (See Klein and Moeschberger Section 13.2). A SAS macro for this procedure is available.

F PROC PHREG

The SAS procedure PHREG is used to perform most of the analyses discussed in this Section. It can be used with a slight modification for either right censored data or for right censored and left truncated data. The general form of the procedure for right censored data is

PROC PHREG options;
MODEL time*censoring(codes) = list of covariate/ options;
STRATA list /option;
Label : TEST hypothesis; (Can be repeated)
Program Statements.;

Here the code in italics is optional while the code in Caps is required. In this case time is the name of the variable containing the on study times, censoring is the name of the variable containing the censoring codes and values in (code) is a list of the codes for <u>censored</u> observation.

For left censored or delayed entry data an alternate form of the model statement is used. Here we say

MODEL (time1,time2)*censoring(codes) =list of covariate/ options;

In this case time1 is the time the subject first becomes at risk and time2 is the time at which the person was last seen. Individuals are in the risk set only for times between time1 and time2.

Before discussing the options for the procedure consider the following two examples of the model statement. For the first suppose that only transplant patients are being analyzed, that the event is overall survival with an on study time of intxsurv and an event indicator of survhi with values of 1 and 3 corresponding to censored observations. Then the model statement is coded as

MODEL intxsurv*survhi(1,3) = list/options;

If we wished to compare transplant to chemotherapy patients, say, then the second form of the model would be used. Suppose the time on study is measured from diagnosis and the variable TSUR holds the time values and the death indicator is DEAD with a value 0 corresponding to a censored observation. BMT patients are left truncated in this model and only become at risk at the time of transplant, while chemotherapy patients are at risk at time 0. We create a time variable ETIME, with value 0 for a chemotherapy patient and a value equal to the waiting time from diagnosis to transplant for a BMT patient . The model statement is now

MODEL (ETIME, TSUR)*DEAD(0) = list of covariate/ options;

Options of primary interest in the PHREG procedure are as follows.
In the PROC statement :
SIMPLE -- Gives the summary statistics for each fixed covariate.
COVOUT OUTEST=data set --Outputs a SAS data set with the parameter estimates and the covariance matrix. This can be inputed into PROC IML to find, for example, relative risks not routinely computed in PHREG.
In the MODEL statement
COVB -0 Prints the covariance matrix of the estimates
RISKLIMITS-- Prints estimates and 95% confidence intervals for the relative risk of each covariate compared to baseline.

ITPRINT--Prints the iteration history. This is important to look at to determine if the numerical routine to estimate the risk coefficients has in fact converged. NOTE SAS will not routinely tell you that there is a problem with convergence.

In the STRATA statement

MISSING -- Tells SAS to have missing as one of the strata. If this is not there SAS will toss out anyone with a missing value for any of the strata.

VI. Modeling 100 Day Mortality

Special techniques are needed to model 100 day mortality (or mortality at any fixed point in time). The techniques in section V are not appropriate since they model the entire survival curve, not the value at a fixed point in time. The approach used to develop a multivariate model parallels that discussed in Section V using a logistic regression model rather than a proportional hazards model.

To model 100 day mortality the data set consists of all individuals who die in the first 100 days and all patients who survive with at least 100 days of follow-up. Any patient with less than 100 days of follow-up who did not die is removed from the data set.

The only covariates that can be modeled are those known at the time of transplant. No time dependent covariates are allowed. Factors are created as discussed in Section V and missing values are handled as discussed there. A single dependent variable is created with a value of 1 if the patient dies in the first 100 days and a value of 0 if they survive 100 days.

The statistical model for the data is the logistic model, namely,

$$\ln\left\{\frac{P[100 \text{ day survival} \mid Z_1, ...,Z_p]}{1-P[100 \text{ day survival} \mid Z_1, ...,Z_p]}\right\} = \beta_1 Z_1 + ...+\beta_p Z_p.$$

In place of the relative risk , the odds ratio is used for 100 day mortality. Here $\exp[\beta_1]$, for example, is the ratio of the odds for an individual with covariate $Z_1 =1$ as compared to the odds for an individual with $Z_1=0$ (and all other covariates the same). More complicated odds ratios can be computed using the formulas in Section V with the relative risk replaced by odds ratio.

Model building for 100 day mortality is identical to that for the Cox model. The exception is that PROC LOGISTIC is used in place of PROC PHREG. The format for the procedure is:

PROC LOGISTIC options;
MODEL Y=list/options;
Label: TEST hypothesis;

Here Y is the indicator of survival at 100 days. Options are identical to those in PROC PHREG.

VII. WRITING COMMITTEE MEMOS

The primary mission of the IBMTR and ABMTR is to bring together data and expertise from many transplant centers to facilitate scientific studies of important issues in hematopoietic stem cell transplantation. IBMTR/ABMTR studies benefit not only from the large numbers of patients available for analysis but, just as importantly, from the diverse talents of participants in the Working/Writing Committees which supervise each study. To derive maximum benefit from this expertise requires good communication between the Statistical Center and the Committees and among Committee members. Face-to-face meetings are infrequent, since members are geographically widely dispersed. The Writing Committee Memo is the primary vehicle for this communication. Writing Committee memos should provide concise information about the status of studies at each stage of progress, allowing Writing Committee members to provide substantive input on all aspects of the study including design, patient population, explanatory and outcome variables, and interpretation of univariate and multivariate analyses. The following is a list of landmarks in a study's course which generally warrant preparation and distribution of a Writing Committee memo. It should not be considered all-inclusive. Writing Committee memos should be prepared whenever substantive deviations from the original study plan are felt to be necessary and/or whenever the Committee's formal input would be beneficial.

(1) Study proposal

The original study proposal submitted for consideration approved should be circulated to the relevant Working Committee(s) once the study is approved, soliciting individuals interested in participating in the Writing Committee. The cover letter for this memo should briefly restate the primary objectives of the study, the intended study population and the initial sample size calculations made when the proposal was considered. The principle investigator should be identified with contact information (address, phone, fax, e-mail). Centers contributing data for large numbers of patients meeting the provisional patient eligibility criteria should be determined. If these centers do not have a representative on the relevant Working Committee(s) for the study, the center director should also receive this memo offering the opportunity to participate on the Writing Committee. This memo should also request suggestions for study design. Example: "The Statistical Center will shortly prepare a protocol (analysis plan) for _____ in collaboration with the (principle investigator). If you have suggestions related to the study design, including patients and outcomes to be studied and variables to be considered, please send these in writing to the (principle investigator) with a copy to the Statistical Center." The memo should include a fax response sheet asking the respondent to indicate whether or not he/she wishes to be part of the Writing Committee and having space for comments.

(2) Study Protocol (See section I)

The Study Protocol should be prepared and reviewed by the principle investigator and then distributed to the Writing Committee, asking for comments. If the comments result in substantive revisions to the protocol, a revised draft should also be circulated.

(3) Description of the study population

The patient eligibility criteria should be clearly defined and patient-, disease-, and treatment-related variables described. Overall outcomes may be included but no univariate or multivariate analyses. Categories of variables for these analyses should be defined.

(4) Univariate analyses/Multivariate analyses

Results should be presented clearly in Table and Figure format with results summarized in the cover letter. Any surprising findings should be highlighted in the cover letter.

(6) Revised analyses

Additional analyses may be performed or other changes to the study done in response to comments from Writing Committee members. These should be presented in table format, with a cover memo addressing each of the comments/criticisms received. It is important that Committee members are notified in writing that their suggestions were taken seriously (as they are) and appropriate action taken.

(7) Manuscript drafts

There will be at least two drafts circulated (often more), the first draft and the draft to be submitted for publication. The latter should include Authorship and Assignment of Copyright forms for signature, if required by the journal to which the paper will be submitted.

(8) Confidentiality

Unpublished data in Writing Committee memos are confidential. Each Writing Committee memo should include the following statement:

"The enclosed data are confidential. If used publicly, the following statement must be included: 'The data presented here were obtained from the IBMTR/ABMTR Statistical Center. The analysis has not been reviewed or approved by the Advisory Committee of the IBMTR or ABMTR. The data may not be published without prior approval of the Advisory Committees.' If the data are used in an oral presentation, please send us the name, place and dates of the meeting where the data are presented, and the title of your presentation."

(9) Authorship

Membership on a Writing Committee is not sufficient for authorship on a manuscript. Each Writing Committee memo should include the following statement:

"You should note that IBMTR/ABMTR rules require that any member of a Writing Committee who does not make a substantive contribution to the design, analysis, interpretation or manuscript withdraw as a co-author or, alternatively, the lead author may remove names of non-contributors."

IBMTR/ABMTR Statisticians' Manual

Appendix A   IBMTR/ABMTR Study Proposal Form

IBMTR
ABMTR

STUDY PROPOSAL GUIDELINES

The rules of the IBMTR/ABMTR state that anyone may propose a study. The person proposing the study must complete a Study Proposal Outline. This is reviewed by the Statistical Center and relevant Working Committee Chair(s). Studies deemed feasible and consistent with the Registries' scientific goals are forwarded to the Working Committee for further input and assignment of a priority score. Studies are initiated at the discretion of the Working Committee Chair, Scientific Director and the Advisory Committee Chair based on priority scores, competing projects and available resources. A Writing Committee is formed to supervise the study. Interested members of the Working Committee and others are permitted to serve on the Writing Committee. To assure co-authorship of the manuscript, members of the Writing Committee must make timely and substantive contributions to study design, data analysis, interpretation of results or preparation of the typescript for publication. Members of the Writing Committee who do not fulfill this requirement are expected to withdraw as a co-author or, alternatively, their names will be deleted by the lead author.

Lead authorship (the person with primary responsibility for the study) is usually the person first proposing a study. The only exception to this policy is, for example, if the person proposing a study has only a trivial proportion of the cases to be studied, while a member of the Working Committee with a large proportion of the patients also requests primary responsibility. When multiple requests for primary responsibility for a single study are received, the person with the largest number of patients in the study is awarded primary responsibility.

The person awarded primary responsibility is required to prepare a first draft of the typescript within 60 days of first receipt of data from the Statistical Center. Failure to do so can result in forfeiture of lead authorship.

IBMTR
ABMTR
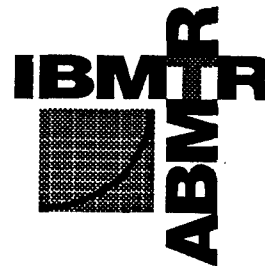
[Name of Study]

STUDY PROPOSAL OUTLINE

Please prepare a brief description (no more than three pages) of the proposed study as you envision it. Use the outline below and send your description to the Statistical Center as soon as possible.

I.   Study Title

II.   Specific Aims

III.   Scientific Justification
        (1-2 paragraphs on the key issues and their importance)

IV.   Patient Eligibility Criteria

V.   Design of Study (Scientific Plan)
        This section should describe how the specific aims will
        be addressed using information from the IBMTR/ABMTR
        database. Carefully review IBMTR/ABMTR data collection
        forms to determine data availability. Include a list of
        variables you believe will be informative and the outcome
        variables you wish to analyze. Specify whether additional
        data would have to be collected and how this would be
        done.
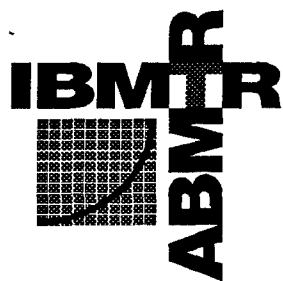
IBMTR/ABMTR Statisticians' Manual

Appendix B   Sample IBMTR/ABMTR Study Protocol

International Bone Marrow Transplant Registry
Autologous Blood & Marrow Transplant Registry
Medical College of Wisconsin
8701 Watertown Plank Road • P.O. Box 26509
Milwaukee, WI 53226 USA

MEDICAL
COLLEGE
OF WISCONSIN

UNRELATED DONOR VERSUS AUTOLOGOUS BONE MARROW TRANSPLANTS FOR ACUTE MYELOGENOUS LEUKEMIA

(NOVEMBER 1996)

STUDY CONTACTS

Mary M. Horowitz, MD, MS
Scientific Director, IBMTR/ABMTR
Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee, WI 53266
Tele: 414-456-8325
Fax: 414-266-8471

Marlies E.H.M. Van Hoef, MD
Visiting Assistant Professor, IBMTR/ABMTR
Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee, WI 53266
Tele: 414-456-8787
Fax: 414-266-8471

Hillard M. Lazarus, MD
University Hospitals of Cleveland
Department of Medicine
11100 Euclid Avenue
Cleveland, OH 44108
Tele: 216-8443629
Fax: 216-844-5979/7406

Craig Kollman, PhD
National Marrow Donor Program
3433 Broadway Street NE, Suite 400
Minneapolis, MN 55413
Tele: 612-627-5820
Fax: 612-627-5899

CO-INVESTIGATORS

James Armitage, MD
Robert Peter Gale, MD, PhD
Rob Geller, MD
Armand Keating, MD
Paul Martin, MD
Carole Miller, MD
Jacob Rowe, MD
Thomas Spitzer, MD
Martin Tallman, MD
Daniel Weisdorf, MD

Table of Contents

1.0 OBJECTIVES

To compare outcome of unrelated donor and autologous bone marrow transplants for acute myelogenous leukemia (AML) in first and second remission. Outcomes to be studied include:

1.1 Hematopoietic recovery;
1.2 Treatment-related mortality;
1.3 Leukemia recurrence;
1.4 Leukemia-free survival;
1.5 Overall survival.

2.0 BACKGROUND

Intensive induction and consolidation chemotherapy has improved the outcome of patients with AML. About 60% of adults and 80% of children achieve complete remission. However, leukemia recurs in 50-70% (1-11). Post-consolidation myeloablative treatment and bone marrow transplantation from an HLA-identical sibling is associated with lower recurrence rates and 50-60% five-year disease-free survival rates for patients transplanted in first remission (12-14). Autologous or unrelated donor transplants are of interest as alternative treatment options, since only 30% of patients have an HLA-identical sibling.

2.1 AUTOLOGOUS TRANSPLANTATION

Treatment-related mortality after autotransplants is about 15% compared to 30% after HLA-identical sibling transplants. Three-year probabilities of survival after autotransplants for AML are 35-60% for patients treated in first remission and 25-35% for patients in second remission (15-22). Relapse rates are higher after autologous transplants compared to HLA-identical sibling transplants. This may be a result of leukemic contamination of the graft and/or lack of graft-versus-leukemia effects. Some data suggest less relapse and better outcome with total body irradiation (TBI) containing regimens (21) and ex vivo purging with mafosfamide (15, 23), 4-hydroxycyclophosphamide (24-26) or monoclonal antibodies (27). Regardless of transplant regimen, relapse (30-50% incidence for patients transplanted in first remission and 40-60% for those transplanted in second remission) is the major cause of treatment failure (18, 20, 22).

2.2 UNRELATED DONOR TRANSPLANTATION

Until recently, use of unrelated donors for transplants was severely limited by availability. Availability increased dramatically over the past five years through establishment of large panels of HLA-typed volunteer donors, such as that maintained by the National Marrow Donor Program (NMDP). Approximately 70% of patients searching the NMDP file find an HLA-A, B and DR antigen matched donor on preliminary searches though fewer actually proceed to

3

transplant. It takes 2-6 months before a suitable donor is identified, evaluated and scheduled for donation. Many patients will relapse in this interval. The few studies that report unrelated donor transplants show lower leukemia-free survival than after HLA-identical sibling transplants. Poorer outcome is attributable to higher treatment-related mortality from graft-versus-host disease (GVHD). The risk of relapse is low, probably due to GVHD-associated graft-versus-leukemia effects (28, 29). In one study from UCLA, matched unrelated donor transplants for high risk AML had two-year leukemia-free survival rates of 23±12%, one-year relapse rates of 24±16% and 57% grade II-IV GVHD (30). The Canadian Bone Marrow Transplant group reported 40% two-year event-free survival after matched unrelated donor transplants for various malignancies (7/35 were AML); most transplants are done in relapse or second or subsequent remission (31). The NMDP recently reported results of 79 AML patients receiving unrelated donor transplants (32). Twenty-five patients, transplanted in first and second remission, had two-year disease-free survival of 40%. Forty percent leukemia-free survival at two years was reported in the low-risk group and 20% in the high-risk group (32). The probability of grade II-IV acute GVHD was 64% and of chronic GVHD 55% (33). This result was consistent with an NMDP report of 462 patients with various malignancies receiving unrelated donor transplants (33). T-cell depletion of donor marrow reduces the incidence of GVHD (25-50%) after unrelated donor transplants (34-37) but does not convincingly increase survival. The Seattle group compared outcome for unrelated donor and autologous transplants in advanced acute leukemia (n=120) (38). There was not a significant difference (p=0.45) in five-year leukemia-free survival. However, only six of 23 unrelated and 11 of 41 autologous transplant recipients with AML were transplanted in second remission and none in first remission.

3.0   PRELIMINARY STUDIES

The Autologous Blood and Marrow Transplant Registry of North America (ABMTR) has collected data on 469 recipients of autotransplants for AML in first or second remission, registered between January 1, 1989 and December 31, 1994. Characteristics of these patients are shown in Table 1.

The NMDP facilitated 163 unrelated donor transplants for AML in first or second remission in the United States during the same period. Characteristics are shown in Table 2.

The International Bone Marrow Transplant Registry (IBMTR) has collected data for 55 unrelated donor transplants for AML in first and second remission, transplanted during the same period in non-USA centers. Characteristics are shown in Table 3.

4

4.0   ANALYSIS PLAN

4.1   ELIGIBILITY CRITERIA

The analysis will include persons receiving autologous or unrelated donor bone marrow transplants for AML in first and second remission between January 1989 and December 1994, with age ≤ 50 years, reported to the ABMTR, IBMTR or NMDP.

4.2   DEFINITION OF ENDPOINTS

The following endpoints will be studied:

4.2.1   Hematopoietic recovery: Time to neutrophils (ANC) > 0.5 x10⁹/L for three consecutive days will be the primary measure for comparisons of hematopoietic recovery.

4.2.2   Leukemia recurrence: Time to first leukemia recurrence will be compared. Patients will be censored at death in continuous complete remission, second transplant or, for patients surviving in continuous complete remission, at last contact.

4.2.3   Leukemia-free survival: Leukemia-free survival is defined as survival in continuous complete remission. Leukemia relapse and death in remission are considered events. Patients surviving in continuous complete remission will be censored at last contact.

4.2.4   Survival: Events are deaths from any cause. Surviving patients are censored at last contact, regardless of intervening treatment.

4.3   POTENTIAL CONFOUNDING VARIABLES

Many factors may affect transplant outcome. Since this is a non-randomized study, careful attention will be paid to potential confounding factors. These are outlined below with suggested categories for analysis.

4.3.1   Patient-related factors
- Age: continuous
- Gender: male vs female
- Karnofsky performance score: < vs ≥ 90%

4.3.2   Disease related factors
- Remission status: first remission (CR1) vs second remission (CR2)
- Cytogenetic abnormalities: t(9;22), -7, -7q, -5, -5q, 11q (±others) vs others vs none vs not tested/available
- FAB classification: FAB M1, 2 vs M3 vs M4 vs M5-7 vs unclassified

- WBC count at diagnosis: < vs ≥ 75 x10^9/L
- Prior treatment: Use of high-dose cytarabine (≥ 1g/m^2/d) during
                             induction/consolidation chemotherapy: yes vs no
                             Time to achieve first remission: < vs ≥ 8 weeks
                             Duration of first remission: < vs ≥ 1 year

4.3.3   <u>Transplant-related factors (allo and auto)</u>
- Year of transplant: continuous variable
- Interval between transplant and most recent remission: continuous
    variable
- Conditioning regimen: TBI-based vs other possible categories
- Growth factors post-transplant: none vs G-CSF/GM-CSF (started within
  72 hours posttransplant)

4.3.4   <u>Transplant-related factors (autologous)</u>
- Marrow purging: yes vs no

4.3.5   <u>Transplant-related factors (allogeneic only)</u>
- GVHD prophylaxis: CsA vs MTX vs CsA+MTX vs T-cell depletion
- Gender-match: male-female vs female-male vs gender-match
- Donor age: continuous
- CMV status donor/recipient: -/- vs -/+ vs +/+ vs +/-
- Donor recipient HLA-match: definition to be determined

4.3.6   <u>Time varying effects</u>

Experience has shown that some of the factors listed in 4.3.1 - 4.3.5 have differential effects on outcome in different time periods. In particular, the primary factor of type of transplant most likely will have different effects in the early and late periods after transplant. This problem is addressed by considering models that allow for distinct relative risks in different time periods.

4.4   DATA RETRIEVAL

The IBMTR/ABMTR statistical center and NMDP will each prepare a data file for patients meeting the eligibility criteria in section 4.1 and including the following variables:

4.4.1   Patient-related variables
- Patient ID number
- Date of birth
- Gender
- Karnofsky performance score pretransplant
- CMV status pretransplant
- Recipient HLA-type (for patients who received an unrelated donor graft)

4.4.2   Disease-related variables
- Date of diagnosis
- Cytogenetics
- FAB classification
- WBC count at diagnosis
- High-dose cytarabine treatment
- Number of induction courses to CR1
- Number of consolidation courses in CR1
- Date of CR1
- Date of first relapse (for CR2 patients)
- Date of CR2 (for CR2 patients)
- Remission state at transplant

4.4.3   Transplant-related variables (allo and auto)
- Date of transplant
- Conditioning regimen
- Center ID number

4.4.4   Transplant-related variables (autologous)
- Bone marrow purging

4.4.5   Transplant-related variables (allogeneic)
- GVHD prophylaxis
- T-cell depletion
- Donor date of birth
- Donor gender
- Donor CMV status
- Donor HLA-type

4.4.6 Follow-up parameters
- Date of achievement of ANC >0.5 x10^9/L as defined in section 4.1.1
- Date of onset acute and chronic GVHD (unrelated only)
- Highest grade of acute and chronic GVHD (unrelated only)
- Date of first posttransplant leukemia recurrence
- Date of death
- Cause of death
- Date of second transplant, if applicable
- Date of last contact

4.5 STATISTICAL METHODS

Patient-, disease- and transplant-related factors will be compared between the two transplant types, using Chi-square test for categorical and Mann-Whitney test for continuous variables.

The data will be analyzed by using a proportional hazards model (39). For this analysis separate models will be fit, using relevant risk factors (section 4.3), to both the autologous and unrelated donor groups. These models will identify variables that require adjustment in each patient group to assure that the comparisons made in later stages are not confounded by other factors. For both of these models the proportional hazards assumption for all variables will be examined using a time-varying covariate and by graphical methods. Factors found to have non-proportional hazards will be adjusted for in subsequent analysis by using a stratified proportional hazards model or by using a set of time-dependent covariates.

Once a set of factors associated with outcome is determined for each of the transplant types, models which directly compare the two types of transplants will be built. A step in this process is to determine if the effect of a given factor is the same for both types of transplants. This will be examined by fitting a proportional hazards model, stratified on transplant type, and examining the interaction term between the factor of interest and the type of transplant. If this interaction term is significant then the final model will have an interaction term between the factor and type of transplant and separate inferences about the effect of transplant type will be made for each level of the confounding factor. The final model constructed by this technique will include all the factors found plus a term for transplant type. The proportional hazards assumption will again be examined, and should it be found that the hazards are non-proportional for the effects of interest, the best fitting model with time-varying risk coefficients will be found. Here the best cut-off point between early and late effects is found by finding the model that yields the largest partial likelihood.

Multivariate regression using partial logistic regression will also be used to compare outcome of autologous and unrelated donor transplants, controlling for

the risk factors identified above (40). Unlike traditional logistic regression, this technique allows for censored data much like a Kaplan-Meier curve or Cox proportional hazards model. The partial logistic model can be very restrictive, imposing conditions analogous to the Cox model, or it can be very flexible, approaching the non-parametric Kaplan-Meier curve as the number of parameters modelled increases. The number of parameters needed will be determined by the fit to the data. A parametric bootstrap will be used to compute confidence intervals and perform tests of significance (41, 42).

4.6   SAMPLE SIZE CALCULATIONS

Table 1 describes 469 patients receiving autotransplants for AML in first and second remission transplanted between January 1989 through December 1994 for whom comprehensive data are available. Three hundred thirty six patients were transplanted in CR1 and 133 in CR2. Table 2 describes the 163 unrelated donor transplants reported to the NMDP in the same period. Sixty one transplants were for AML in CR1 and 102 for AML in CR2. Table 3 describes the 55 non-USA unrelated donor transplants reported to the IBMTR in the same period. Twenty four transplants were for AML in CR1 and 31 for AML in CR2.

Tables 4 and 5 show the power to detect specified differences in leukemia-free survival with autologous versus unrelated donor transplants, assuming inclusion of all unrelated donor transplants reported to either NMDP or IBMTR (Tables 2 and 3). The displayed data are based on the assumption that 50% of autotransplant recipients for AML in CR1 and 30% of those with AML in CR2 are alive and disease-free three years post-transplant (non-published data from ABMTR). It must be noted that the probability of detecting a difference between treatment groups with given power depends on the amount of censoring and variation in risk factors between the groups. This may induce potential discrepancies that interfere with the power calculations.

5.0 REFERENCES

1. Mayer RJ, Davis RB, Schiffer CA, et al. Intensive postremission chemotherapy in adults with acute leukemia. N Eng J Med 1994;331:896-903.
2. Champlin RE, Gale RP. Acute myelogenous leukemia: Recent advances in therapy. Blood 1987;69:1551-1562.
3. Miescher PA, Jaffe ER, Gale RP (eds). Keystone Symposia Workshop: Curing Leukemia. Semin Hematology 1991;28(suppl 4).
4. Weinstein HJ, Mayer RJ, Rosenthal DS, et al. Chemotherapy for acute myelogenous leukemia in children and adults: VAPA update. Blood 1983;62:315-319.
5. Creutzig U, Ritter J, Riehm H, et al. The childhood AML studies BFM-78 and -83: Treatment results an risk factor analysis. In: Acute leukemias: Prognostic factors and treatment strategies (ed. by T. Buchner, G Schellong, W Hiddemann, et al) pp. 71-75, Springer, Berlin, 1987.
6. Amadori S, Ceci A, Comelli A, et al. Treatment of acute myelogenous leukemia in children. Results of Italian cooperative study AIEOP/LAM 8204. J Clin Oncol 1987;5:1356-1363.
7. Mandelli F, Petti MC, Spiriti MA, et al. Acute non-lymphoid leukemia treatment: an update. Haematologica 1988;73:1-6.
8. Dillman RO, Davis RB, Green MR, et al. A comparative study of two different doses of cytarabine for acute myeloid leukemia: a phase III trial of cancer and leukemia group B. Blood 1991;78:2520-2526.
9. Wiernik PH, Banks PLC, Case Jr DC, et al. Cytarabine plus idarubicin or daunorubicin as induction and consolidation therapy for previously untreated adult patients with acutte myeloid leukemia. Blood 1992;79:313-319.
10. Schiller GJ, Nimer SD, Territo MC, et al. Bone marrow transplantation versus high-dose cytarabine-based consolidation chemotherapy for the treatment results in childhood acute myelogenous leukemia: A report of the German Cooperative Study AML-BFM-78. Blood 1985;65:298-304.
11. Phillips GL, Reece DE, Shepherd JD, et al. High-dose cytarabine and daunorubicin induction and post-remission chemotherapy for the treatment of acute myelogenous leukemia in adults. Blood 1991;77:1429-1435.
12. International Bone marrow Transplant registry. Transplant or chemotherapy in acute myelogenous leukemia. Lancet 1989;1:1119-1122.
13. Clift RA, Buckner CD, Thomas ED, et al. The treatment of acute non-lymphoblastic leukemia by allogeneic marrow transplantation. Bone marrow Transplant 1987;2:243-258.
14. European Group for Bone Marrow transplantation: Working party on Leukemia. Allogeneic bone marrow transplantation of leukemia in Europe. Lancet 1988;1:1379-1382.
15. Gorin NC, Aegerter P, Auvert B, et al. Autologous bone marrow transplantation for acute myelocytic leukemia in first remission: a European survey of the role of marrow purging. Blood 1990;75:1606-1614.
16. Lowenberg B, Verdonck LJ, Dekker AW, et al. Autologous bone marrow transplantation in first remission: results of a Dutch prospective study. J Clin Onocl 1990;8:287-294.
17. McMillan AK, Goldstone AH, Linch DC, et al. High-dose chemotherapy and autologous bone marrow transplantation in acute leukemia. Blood 1990;76:480-488.

18. Carella AM, Gaozza E, Santini G, et al. Autologous unpurged bone marrow transplantation for acute non-lymphoblastic leukemia in first complete remission. Bone Marrow Transplant 1988;3:537-541.

19. Spinolo JA, Dicke KA, Horowitz, et al. Double intensification with amsacrine/high-dose cytarabine and high-dose chemotherapy with autologous bone marrow transplantation produces durable remission in acute myelogenous leukemia. Bone marrow transplant 1990;5:111-118.

20. Korbling M, Hunstein W, Fliedner TM, et al. Disease-free survival after autologous bone marrow transplantation in patients with acute myelogenous leukemia. Blood 1989;74:1898-1904.

21. Labopin M, Gorin NC. Autologous marrow transplantation in 2502 patients with acute leukemia in Europe: a retrospective study. Leukemia 1992;6(suppl 4):95-99.

22. Ravindranath Y, Yeager AM, Chang MN, et al. Autologous bone marrow transplantation versus intensive consolidation chemotherapy for acute leukemia in childhood.

23. Korbling M, Fliedner TM, Holle R, et al. Autologous blood stem cell (ABSCT) versus purged bone marrow transplantation (pABMT) in standard risk AML: influence of source and cell composition of the autograft on hemopoietic reconstitution and disease-free survival. Bone marrow transplant 1991;7(5):343-349.

24. Rowley SD, Jones RJ, Piantadosi S, et al. Efficacy of ex vivo purging for autologous bone marrow transplantation for acute myeloid leukemia using monocolonal antibocy-purged bone marrow. Blood 1990;75:1199-1206.

25. Linker CA, Ries CA, Damon LE, et al. Autologous bone marrow transplantation for acute myeloid leukemia using busulphan plus etoposide as a preparative regimen. Blood; 1993:81(2):311-318.

26. Dusenbery KE, Daniels KA, McClure JS, et al. Randomized comparison of cyclophosphamide-total body irradiation versus busulphan-cyclophosphamide conditioning in autologous bone marrow transplantation for acute myeloid leukemia. Int J Radiol Oncol 1995;31(1):119-128.

27. Ericson SG, Colby E, Welch L, et al. Engraftment of leukocyte subsets following autologous bone marrow transplantation in acute myeloid leukemia using anti-myeloid (CD14 and CD15) monoclonal antibody-purged bone marrow. Bone Marrow Transplant 1992;9(2):129-137.

28. Beatty PG. Results of allogeneic bone marrow transplantation with unrelated or mismatched donors. Semin in Oncol 1992;19(3 suppl 7):13-19.

29. Beatty PG. Results of allogeneic bone marrow transplantation with unrelated or mismatched donors. Semin in Oncol 1992;19(3 suppl 7):13-19.

30. Schiller G, Feig SA, Territo M, et al. Treatment of advanced leukemia with allogeneic bone marrow transplantation from matched unrelated donors. Br J Haematol 1994;88(1):72-78.

31. Phillips GHL, Burnett MJ, Brain MC, et al. Allogeneic bone marrow transplantation using unrelated donors: a pilot study of the Canadian bone marrow transplant group. Bone Marrow Transplant 1991;8(6):477-487.

32. Perkins HA, Kollman C, Howe CW. Unrelated-donor marrow transplants: the experience of the national Marrow Donor Program. Clin Transplants 1994;295-301.

33. Kernan NA, Bartsch G, Ash RC, et al. Analysis of 462 transplantations from unrelated donors facilitated by the National Donor Marrow Program. N Eng J Med 1993; 328(9):593-602.

34. Cullis JO, Szydlo RM, Cross NCP, et al. Matched unrelated donor bone marrow transplantation for chronic leukemia in chronic phase: comparison of ex vivo and in vivo T-cell depletion. Bone Marrow Transplant 1993; 11 (Suppl 1):107.

35. Mackinnon S, Hows JM, Goldman JM, et al. Bone marrow transplantation for chronic myeloid leukemia: The use of histocompatibility unrelated volunteer donors. Exp Hematol 1990;18:421.

36. Drobyski WR, Ash RC, Casper JT, et al. Effect of T-cell depletion as GVHD prophylaxis on engraftment, relapse and disease-free survival in unrelated marrow transplantation for chronic myelogenous leukemia. Blood 1994;83:1980.

37. Ash RC, Casper JT, Chitambar CR, et al. Successfull allogeneic transplantation of T-cell depleted bone marrow from closely HLA-matched unrelated donors. N Eng J Med 1990;322:485.

38. Busca A, Anasetti C, Anderson G, et al. Unrelated donor or autologous transplantation for treatment of acute leukemia. Blood 1994;83:3077-3084.

39. Andersen PK, Bogan O, Gill RD, et al. Statistical Models Based on Counting Processes. Springer Verlag, New York 1992.

40. Efrom B. Bootstrap Confidence Intervals for a Class of parametric problems. Biometrika 1985;72:45-58.

41. CiCiccio TJ, Romano JP, et al. A review of Bootstrap Confidence Intervals. J of Royal Statist Soc 1988;50(3):338-354.

42. Cox RD. Regression analysis and life tables. J of Royal Statist Soc 1972;B 34:187-220.

Table 1. Characteristics of patients with AML in CR1 and CR2, who received autologous bone marrow transplantation and for whom comprehensive data are available.

Variable	CR1 (%)[a] median (range)[b]	CR2 (%)[a] median (range)[b]
Number of patients	336	133
Year of transplant		
1989	45 (13)	25 (19)
1990	50 (15)	28 (21)
1991	81 (24)	22 (17)
1992	73 (22)	29 (22)
1993	80 (24)	26 (20)
1994	7 (2)	3 (2)
Age in years	25 (1-65)	32 (1-63)
Male sex	164 (49)	73 (55)
Karnofsky performance score ≥ 90%	282 (84)	97 (73)
WBC at diagnosis (x10^9/l)	8 (1-690)	7 (1-479)
FAB		
M1	50 (15)	26 (20)
M2	92 (27)	42 (32)
M3	35 (10)	13 (10)
M4	66 (20)	36 (27)
M5	49 (15)	7 (5)
M6	---	---
M7	6 (2)	2 (2)
Unclassified	22 (7)	7 (5)
Granulocytic sarcoma	16 (5)	16 (5)
Conditioning regimen		
BU + CY ± other	236 (70)	93 (70)
TBI + CY ± other	21 (6)	19 (14)
TBI + other	31 (9)	9 (7)
BU ± other	13 (4)	3 (2)
CY + VP16 + nitrosurea	20 (6)	3 (2)
Graft purged	198 (60)	92 (70)
Missing[c]	5 (1)	2 (2)

[a] for categorical variables, [b] for continuous variables, [c] data are only missing for purging
Abbreviations: WBC=white blood count; FAB=French-American-British; BU=busulfan; CY=cyclophosphamide; TBI=total body irradiation

Table 2.   Characteristics of unrelated donor transplants for AML in CR1 and CR2 from the NMDP.

Variable	CR1 (%)[a] median (range)[b]	CR2 (%)[a] median (range)[b]
Number of patients	61	102
Year of transplant		
1989	3 (5)	4 (4)
1990	7 (11)	10 (10)
1991	7 (11)	24 (23)
1992	12 (20)	15 (15)
1993	15 (25)	16 (16)
1994	17 (28)	33 (32)
Age in years	25 (0-48)	26 (0-55)
Male sex	43 (71)	62 (61)
Karnofsky Performance score ≥90%	52 (85)	77 (75)
Conditioning regimen		
Bu + CY	12 (20)	16 (16)
TBI + CY	-	-
TBI + CY + other	32 (53)	58 (57)
TBI + other	3 (5)	7 (7)
TBI + Cy + Arac	9 (15)	12 (12)
TBI + Cy + VP16	5 (8)	9 (9)
GVHD prophylaxis		
CsA	1 (2)	3 (3)
CsA + other, no MTX	2 (3)	9 (9)
CsA + MTX	27 (44)	52 (51)
T-cell depletion	-	-
T-cell depletion + other	25 (41)	28 (27)
Other	6 (10)	10 (10)
Donor male sex	31 (51)	65 (64)
Donor age	35 (20-52)	37 (21-55)

[a] for categorical variables, [b] for continuous variables.
Abbreviations: BU=busulfan; CY=cyclophosphamide; TBI=total body irradiation; CsA=cyclosporin; MTX=methotrexate

Table 3. Characteristics of unrelated donor transplants for AML in CR1 and CR2 reported to the IBMTR.

Variable	CR1 (%)[a] median (range)[b]	CR2 (%)[a] median (range)[b]
Number of patients	24	31
Year of transplant		
1989	2 (8)	3 (10)
1990	3 (13)	3 (10)
1991	2 (8)	7 (23)
1992	5 (21)	8 (26)
1993	6 (25)	3 (10)
1994	6 (25)	7 (23)
Age in years	20 (1.3-50)	25 (3.6-46)
Male sex	14 (58.3)	16 (51.6)
Karnofsky Performance score ≥90%	17 (70.8)	25 (80.6)
WBC at diagnosis (x10^9/L)	9.6 (1.3-210)	6.3 (0.7-199)
missing	1 (4)	2 (6)
FAB		
M1	5 (21)	5 (16)
M2	3 (13)	8 (26)
M3	-	10 (32)
M4	7 (29)	4 (13)
M5	5 (21)	3 (10)
M6	4 (17)	-
unclassified	-	1 (3)
Conditioning regimen		
Bu + CY	4 (17)	2 (6)
TBI + CY	9 (38)	10 (32)
TBI + CY + other	6 (25)	9 (29)
TBI + other	-	1 (3)
TBI + Cy + Arac	-	2 (6)
TBI + Cy + VP16	4 (17)	5 (16)
Other	1 (4)	2 (6)
GVHD prophylaxis		
CsA	1	3 (10)
CsA + other, no MTX	1	2 (6)
CsA + MTX	17	18 (26)
T-cell depletion	1	1 (3)
T-cell depletion + other	4	7 (23)
Donor male sex	35.9 (0.4-50)	35 (21-56)
Donor age	14 (58.3)	20 (64.5)

[a] for categorical variables, [b] for continuous variables. Abbreviations: BU=busulfan; CY=cyclophosphamide; TBI=total body irradiation; CsA=cyclosporin; MTX=methotrexate

Table 4.   Power to detect a difference in leukemia-free based on 50% 3-year leukemia-free survival in 336 evaluable autologous transplants (H_0) and 85 evaluable unrelated donor transplants (H_a) for AML in first remission.

H_a	Difference in LFS (%)	Power	H_a	Difference in LFS (%)	Power
55	5	0.1290	45	5	0.1290
60	10	0.3845	40	10	0.3845
65	15	0.7127	35	15	0.7127
70	20	0.9258	30	20	0.9258
75	25	0.9912	25	25	0.9912
80	30	0.9996	20	30	0.9996

H_a = assumed LFS in unrelated donor transplants

Table 5.   Power to detect a difference in leukemia-free based on 30% 3-year leukemia-free survival in 133 evaluable autologous transplants (H_0) and 133 evaluable unrelated donor transplants (H_a) for AML in second remission.

H_a	Difference in LFS (%)	Power	H_a	Difference in LFS (%)	Power
35	5	0.1377	25	5	0.1474
40	10	0.4015	20	10	0.4714
45	15	0.7171	15	15	0.8418
50	20	0.9177	10	20	0.9874
55	25	0.9863	5	25	0.9999
60	30	0.9988			

H_a = assumed LFS in unrelated donor transplants
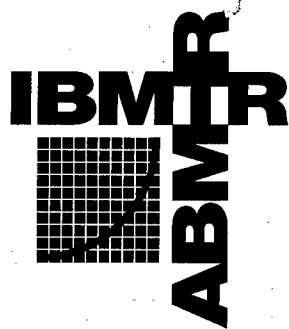
Autologous Blood & Marrow Transplant Registry

ABMTR Newsletter

December 1997	Volume 4, Number 1

A reminder of our new fax # (414) 456-6530

Table of Contents:

The ABMTR Newsletter is funded by an unrestricted educational grant from ICN Pharmaceuticals, Inc.

MEDICAL COLLEGE OF WISCONSIN

COMMUNITY RESPIRATORY VIRAL INFECTIONS IN THE POSTTRANSPLANT PATIENT

by Richard E. Champlin, MD
M. D. Anderson Cancer Center, Houston, Texas

Infection is a common and often life-threatening problem in the first year after blood and bone marrow transplantation. Multiple bacterial, fungal and viral organisms are implicated, many not serious pathogens except in settings of compromised immune function. Strategies for preventing and treating gram-negative and gram-positive bacterial infections, fungal infections and herpes virus infections such as cytomegalovirus receive much attention; improved management of these infections contributes to recent decreases in transplant-related mortality. The importance of common respiratory viruses, such as respiratory syncytial virus (RSV), influenza, parainfluenza, rhinoviruses, adenoviruses and coronaviruses, in causing severe illness in transplant recipients is less well understood.

IBMTR/ABMTR ANNUAL PARTICIPANTS' MEETING in Keystone, Colorado on January 8-14, 1998

by D'Etta Waldoch Severson, CMP, IBMTR/ABMTR Associate Director-International Programs

The 1998 Annual Participants' Meeting will combine a stimulating scientific program, 13 Working Committee meetings, a beautiful venue and some of the best skiing available in Colorado. Plenary and Simultaneous Scientific Sessions will be presented by more than 75 speakers representing 10 countries. Topics include evaluation of minimal residual disease, ex vivo expansion of stem cells, biology of dendritic cells, immunotherapy in the transplant setting, cord blood and peripheral blood allografts and posttransplant infections. Sessions will be held in the morning and evening, allowing time in the afternoon for participants to enjoy a variety of winter recreational activities at Keystone.

The 1998 Keynote Address, *The Other Side of Health Care—A Physician Treated by Transplantation*, will be given by Dr. Richard Boxer on Sunday, January 11, at the opening reception. Dr. Boxer, a national leader in health care reform and a practicing urologist, received an autotransplant for non-Hodgkin lymphoma at the University of Nebraska in Omaha. On Monday, January 12, the late afternoon reception will be combined with an IBMTR/ABMTR Poster Session. The $500 Mortimer M. Bortin Research Award will be given for the best abstract submitted.

Data Management Workshops will be held on Friday, January 9. Sessions on scoring common toxicities, and overviews of statistical analyses, high-dose therapies and audit survival tactics will provide practical guidelines for those working with clinical data and the Statistical Center. $500 grants from the US Department of Defense will be awarded to 30 eligible data managers to offset travel costs associated with attending the Workshops. StemCell Technologies Inc will offer three full-day training sessions at Keystone, January 10-12. The fee for participating in each session is $400. Those interested may contact Ellen Low at ☎ 800-667-0322 or ☎ 604-877-0713, or stemsoft@stemcell.com.

Friday evening and Saturday, January 9-10, are devoted to a series of excellent corporate-supported Satellite Sessions. Breakfast on Sunday, Monday and Tuesday will feature Satellite Poster Sessions, and a luncheon Satellite Session will be held on Monday.

For meeting information, contact D'Etta at the Statistical Center: ☎ 414-456-8377 or fax: 414-456-6530

The IBMTR/ABMTR Steering Committees will meet for the first time at Keystone, as well as the Executive, Advisory and Working Committees. The five-day meeting will conclude on Wednesday, January 14, at noon.

Register Early!
More than 500 participants are expected to attend the 1998 Annual Meeting at Keystone. Participants are encouraged to make hotel reservations soon.

The ABMTR Continues As a Unique Resource for Studying the Growing Use of Autologous Transplantation

The Autologous Blood & Marrow Transplant Registry (ABMTR) continues to grow. Currently, 220 participating centers in the United States, Canada, Mexico and South America provide data to the Registry. More than 100 physicians from these centers volunteer their time to serve on one or more ABMTR Working Committees, to plan and conduct studies using these data.

In the past year, ABMTR centers registered over 7,000 new patients. The total number of transplants available for study exceeds 30,000. The distribution of diseases treated by those transplants is shown below.

These data are being used to conduct an increasing number of studies. The ABMTR has active investigations in autotransplants for breast cancer, non-Hodgkin and Hodgkin lymphoma and ovarian cancer. Disease-specific Report Forms are recently complete or near completion for multiple myeloma, neuroblastoma, lung cancer and CNS tumors. Data col-

lected on these forms will allow additional studies in the near future. The Registry continues to be a unique resource for studying the impact of high-dose therapy on management of patients with diverse disorders.

This issue of the Newsletter focuses on RSV (respiratory syncytial virus) and other community respiratory viral infections in the bone marrow transplant setting, an increasingly recognized problem in immune suppressed patients. Understanding the epidemiology and manifestations of these infections in the posttransplant patient is important to allow early treatment. Registry studies to provide insight into the prevalence and natural history of community respiration infections are planned. The Newsletter also summarizes a new ABMTR study on autotransplants for neuroblastoma, funded in part by the Eppley Foundation for Research in New York.

On behalf of the Registry, I want to express thanks to all those whose efforts make this program a success.

Distribution of autotransplants performed between 1989 and 1996, registered with the ABMTR by 220 teams in North and South America

Disease	Totals, %
Breast cancer	10,556 (35)
Non-Hodgkin lymphoma	7,653 (25)
Hodgkin lymphoma	3,593 (12)
Acute myelogenous leukemia	2,330 (8)
Acute lymphoblastic leukemia	590 (2)
Chronic myelogenous leukemia	271 (1)
Multiple myeloma	1,715 (6)
Neuroblastoma	735 (2)
Ovarian cancer	695 (2)
Testicular cancer	452 (1)
Brain tumor	370 (1)
Lung cancer	128 (<1)
Bone sarcoma	118 (<1)
Other cancer	1,189 (4)
Total	**30,395**

The IBMTR/ABMTR Statistical Center Celebrates Achievements: 1972-1997

This year was a very special one for the IBMTR/ABMTR Statistical Center. First, we celebrated the 25th anniversary of the IBMTR. On September 13 over 200 physicians and scientists from around the world joined us at the Medical College of Wisconsin for our 25th Anniversary Educational Symposium on *New Directions in Blood Cell and Bone Marrow Transplants*. Speakers addressed issues of stem biology, alternative sources of stem cells for transplantation, gene therapy and xenotransplantation. Almost 300 friends and supporters shared a gala dinner program that evening, featuring comments by Dan Rutz of CNN News and a keynote speech by Wisconsin First Lady Sue Ann Thompson (see p. 6). We were very pleased to have three of the IBMTR's founders join us for the celebration: Dr. Robert Good of All Children's Hospital, St. Petersburg, Florida; Professor Georges Mathé of the Institut de Cancerologie et d'Immunologie, Villejuif, France; and Dr. George W. Santos of The Johns Hopkins University School of Medicine, Baltimore, Maryland.

Second, I am happy to announce, the National Institutes of Health intends to award an R24 grant to support the IBMTR and ABMTR for 1998-2003. This grant will provide about 60 percent of the funds needed for our scientific and educational programs. The remaining funds must come from foundation, corporate and individual donations.

Third, accrual to the database reached an all-time high. The Statistical Center received about 7,000 initial Report Forms for transplant recipients during the past year, an increase of more than 2,000 compared to the year before!

Finally, five IBMTR/ABMTR studies were accepted for presentation at this year's annual meeting of the American Society of Hematology (ASH), December 5-9, 1997, San Diego, California:

Dr. Julie Vose (University of Nebraska, Omaha) will present results of autotransplants in patients with aggressive non-Hodgkin lymphoma failing primary induction therapy. This study of 221 patients failing to achieve a first complete remission with conventional therapy demonstrates 100-day mortality of $17 \pm 5\%$ (95% confidence interval) with 3-year progression-free and overall survival of $32 \pm 6\%$ and $40 \pm 7\%$, respectively. The only predictor of autotransplant outcome was sensitivity to prior chemotherapy. Patients with resistant disease had a 3-year probability of survival of only $19 \pm 12\%$ compared to $48\% \pm 13\%$ for those with sensitive (partial response) disease.

Dr. Martin S. Tallman (Northwestern University, Chicago) will present a study of the effect of high-dose cytarabine, given for consolidation of acute myelogenous leukemia in first remission, on outcome of subsequent HLA-identical sibling transplants. The study includes 77 patients receiving no postremission therapy prior to transplant, 151 receiving high-dose cytarabine and 239 receiving other consolidation therapy including cytarabine at standard dose. Preliminary analyses indicate no differences in relapse, transplant-related mortality or survival.

Dr. Stella Davies (University of Minnesota, Minneapolis) will present a comparison of total body irradiation (TBI) or busulfan with cyclophosphophamide for pretransplant conditioning in children transplanted in first or second remission. Multivariate analyses show increased treatment-related mortality and lower leukemia-free survival in the children receiving TBI.

Dr. Jakob Passweg (Kantonsspital Basel, Switzerland) will present an analysis of bone marrow transplant for severe aplastic anemia using unrelated or HLA-mismatched related donors. Five-year probabilities of survival in this cohort of 240 patients transplanted between 1985 and 1995 are $37 \pm 7\%$.

Dr. Philip Rowlings (Medical College of Wisconsin, Milwaukee) will present 8 cases of Hodgkin Disease developing after an allogeneic bone marrow transplant for leukemia or aplastic anemia. The observed-to-expected (in the general population) incidence ratio of Hodgkin Disease in transplant recipients was 6.31 (95% confidence interval 2.7-12). In contrast to other posttransplant lymphoproliferative disorders, these tumors developed relatively late and were not associated with T-cell depletion of donor marrow, use of antilymphocyte globulin or donor-recipient mismatch. In situ hybridization studies suggested presence of Epstein Barr virus in at least half of these cases.

These studies indicate the diversity and importance of issues addressed using the IBMTR/ABMTR database. Thank you for your continued participation in IBMTR/ABMTR research and educational programs. Through your help, we have been able to make a significant impact on the success of blood and marrow transplantation over the past 25 years.

Mary M. Horowitz,
MD, MS
Scientific Director

Mary M. Horowitz, MD, MS is Scientific Director of the IBMTR/ABMTR and Professor of Medicine at the Medical College of Wisconsin

ABMTR INITIATES STUDY OF AUTOTRANSPLANTS FOR NEUROBLASTOMA

By Philip A. Rowlings, MD, MS, IBMTR/ABMTR Assistant Scientific Director

Neuroblastoma is the most common extra-cranial solid tumor of children accounting for 8%-10% of childhood malignancies. In the United States, between 500 and 1,000 children are diagnosed with neuroblastoma each year. Eighty-five percent are less than six years old at the time of diagnosis. Stage of disease and age at diagnosis are the major determinants of treatment outcome. Clinical staging of neuroblastoma is based on the extent of the primary tumor and sites of metastases. A set of uniform criteria for diagnosis, staging, and response to therapy were recently published (1). About 40% of children are cured with surgery, radiation and/or chemotherapy. Conventional treatments fail in the remaining 60%.

Published results of autotransplants in relatively small numbers of patients with high risk neuroblastoma are encouraging, showing disease-free survival rates of 30-50% (2). The ABMTR database has information for over 700 autotransplants for neuroblastoma. By analyzing large numbers of patients, the study should provide a more precise estimate of outcome in groups defined by well-characterized prognostic factors.

The study will also examine patient-, disease- and treatment-related variables for their association with transplant outcome. Of particular interest is the relative efficacy of high-dose conditioning regimens and approaches to graft purging. Also, because ABMTR centers provide continuing follow-up information on long-term survivors, the study will attempt to define the risk of late effects such as second cancers. In collaboration with the Pediatric Oncology Group, a quality of life questionnaire will also be developed to assess functional status of long-term survivors of autotransplants for neuroblastoma. Finally, in collaboration with the IBMTR, the study will compare the outcome of autologous and allogeneic transplants for neuroblastoma.

The first step in this study, development of a Disease-Specific Report Form for data collection was recently completed, with the help of a generous grant from the New York-based Eppley Foundation for Research. Centers who have submitted information regarding their neuroblastoma patients on older versions of the Report Forms will be asked to submit a supplemental form to provide all of the information required for the planned studies. We encourage you to submit the brief supplemental form as quickly as possible.

The study, which is under the auspices of the IBMTR/ABMTR Pediatric Cancer Working Committee (Chair, Bruce Camitta), will be chaired by Naynesh R. Kamani, MD, Director, Pediatric Bone Marrow Transplantation at the University of Texas Health Science Center in San Antonio. Individuals who wish to participate in this study or have questions may contact the IBMTR/ABMTR Statistical Center or Dr. Naynesh Kamani, Director, Pediatric Bone Marrow Transplantation, Division of Hematology/Oncology/Immunology, The University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284, ☎ (210) 704-3450 or fax (210) 704-2396, email: nkamani@srhcc.org.

1. Brodeur G, Pritchard J, Berthold F, et al. Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment. J Clin Oncol 11:1466-1477, 1993.

2. Kamani NR. Autotransplants for neuroblastoma. Bone Marrow Transplant 17:301-304, 1996.

RECENT SCIENTIFIC REPORTS FROM THE IBMTR/ABMTR

Curtis RE, Rowlings PA, Deeg HJ, Shriner DA, Socié G, Travis LB, Horowitz MM, Witherspoon RP, Hoover RN, Sobocinski KA, Fraumeni JF Jr, Boice JD Jr. **Solid cancers after bone marrow transplantation.** New Engl J Med 336:897-904, 1997.

Szydlo R, Goldman JM, Klein JP, Gale RP, Ash RC, Bach FH, Bradley BA, Casper JT, Flomenberg N, Gajewski JL, Gluckman E, Henslee-Downey PJ, Hows JM, Jacobsen N, Kolb H-J, Lowenberg B, Masaoka T, Rowlings PA, Sondel PM, van Bekkum DW, van Rood JJ, Vowels MR, Zhang MJ, Horowitz MM. **Results of allogeneic bone marrow transplants for leukemia using donors other than HLA-identical siblings.** J Clin Oncol 15:1767-1777, 1997.

Antman KH, Rowlings PA, Vaughan WP, Pelz CJ, Fay JW, Fields KK, Freytes CO, Gale RP, Hillner BE, Holland HK, Kennedy MJ, Klein JP, Lazarus HM, McCarthy PL Jr, Saez R, Spitzer G, Stadtmauer EA, Williams SF, Wolff S, Sobocinski KA, Armitage JO, Horowitz MM. **High-dose chemotherapy with autologous hematopoietic stem cell support for breast cancer in North America.** J Clin Oncol 15:1870-1879, 1997.

Passweg JR, Socié G, Hinterberger W, Bacigalupo A, Biggs JC, Camitta BM, Champlin RE, Gale RP, Gluckman E, Gordon-Smith EC, Hows JM, Klein JP, Nugent ML, Pasquini R, Rowlings PA, Speck B, Tichelli A, Zhang MJ, Horowitz MM, Bortin MM. **Bone marrow transplantation for severe aplastic anemia: Has outcome improved?** Blood 90:858-864, 1997.

Zhang MJ, Baccarani M, Gale RP, McGlave PB, Atkinson K, Champlin RE, Dicke KA, Giralt S, Gluckman E, Goldman JM, Klein JP, Herzig RH, Masaoka T, O'Reilly RJ, Rozman C, Rowlings PA, Sobocinski KA, Speck B, Zwaan FE, Horowitz MM. **Survival of patients with chronic myelogenous leukaemia relapsing after bone marrow transplantation: Comparison with patients receiving conventional chemotherapy.** Br J Haematol, 1997. In press.

Lee SJ, Kuntz KM, Horowitz MM, McGlave PB, Goldman JM, Sobocinski KA, Hegland J, Kollman C, Parsons SK, Weinstein MC, Weeks JC, Antin JH. **A decision analysis of unrelated donor bone marrow transplantation for chronic myelogenous leukemia.** Ann Int Med, 1997. In press.

Gale RP, Hehlmann R, Zhang MJ, Hasford J, Goldman JM, Heimpel H, Hochhaus A, Klein JP, Kolb H-J, McGlave PB, Passweg JR, Rowlings PA, Sobocinski KA, Horowitz MM and the German CML Study Group. **Survival with bone marrow transplantation versus hydroxyurea or interferon for chronic myelogenous leukemia.** Blood, 1997. In press.

Waters TM, Bennett C, Pajeau TS, Sobocinski KA, Klein JP, Rowlings PA, Horowitz MM. **Economic analyses of bone marrow and blood stem cell transplantation for leukemias and lymphoma: What do we know?** Bone Marrow Transplant, 1997. In press.

Passweg JR, Tiberghein P, Cahn J-Y, Vowels MR, Camitta BM, Gale RP, Herzig RH, Hoelzer D, Horowitz MM, Ifrah N, Klein JP, Marks DI, Ramsay NKC, Rowlings PA, Weisdorf DJ, Zhang MJ, Barrett AJ. **Graft versus leukemia effects in T-lineage and B-lineage acute lymphoblastic leukemia.** Bone Marrow Transplant, 1997. In press.

Reprints available on request

Infection with community respiratory viruses in immune competent persons is common though generally not serious, the most frequent syndrome being the "common cold." Except in the elderly and newborn, community respiratory virus infections generally involve only the upper respiratory tract and are self-limited in immune competent individuals.

A recent study at the M.D. Anderson Cancer Center (MDACC), examining nasal and throat specimens in leukemia and transplant patients presenting with respiratory symptoms, demonstrated community respiratory viruses in 27%. Viral prevalence in this study mirrored that in the community except that RSV was more common than might be expected. RSV was, in fact, the most common respiratory virus isolate. RSV infections occurred primarily in the winter and early spring. In contrast to respiratory virus infections in immune competent persons, such infections in transplant recipients frequently progressed to pneumonia after an upper respiratory prodrome. In MDACC studies, RSV was associated with pneumonia in about half of patients infected in the first year after an allogeneic bone marrow transplant; more than half of RSV pneumonias were fatal.

Strategies for preventing morbidity and mortality from community respiratory viruses require better awareness of their prevalence, prevention of nosocomial transmission, im-

munization and early diagnosis and treatment. Several studies demonstrate that respiratory viruses are frequently transmitted nosocomially, often from persons with only mild symptoms of illness. Strict adherence to infection control measures, that include contact isolation and prevention of exposure to persons with even mild respiratory illnesses,

> *"...successful treatment [of community respiratory virus infections] requires early diagnosis and intervention."*

can decrease nosocomial risk. Immunization is available only for influenza virus; patients, family members and health care workers should be vaccinated yearly. Passive immunization with immune globulin may be helpful for some viruses, including RSV. Effective antivirals are available for influenza A (amantadine, rimantidine) and RSV (ribavirin). However, successful treatment requires early diagnosis and intervention. This requires awareness of the prevalence of these viruses in the community and appropriate investigation of respiratory symptoms.

Although it is well-proven that community respiratory viruses can cause severe pulmo-

nary infection and death in transplant recipients, their overall contribution to early and late mortality after blood and marrow transplantation is still unclear. Most studies are limited by small numbers, inadequate sampling and restriction to patients with severe respiratory symptoms. The IBMTR/ABMTR will be exploring this area over the next few years, first by examining the seasonal incidence of fatal and non-fatal respiratory infections. We are particularly interested in whether interstitial pneumonias reported as idiopathic are associated with known patterns of viral prevalence in the community. With better understanding of the natural history of these disorders, hopefully progress can be made in prevention, diagnosis and treatment strategies.

Suggested Reading:

Whimbey E, Englund JA, Ljungman P (ed). Proceedings of a Symposium: Community respiratory viral infections in the immunocompromised host. Am J Med 1997;102 (3A).

Whimbey E, Champlin RE, Couch RB, et al. Community respiratory virus infections among hospitalized adult bone marrow transplant recipients. Clin Infect Dis 1996;22:778-782.

Wendt CH, Hertz MI. Respiratory syncytial virus and parainfluenza virus infections in the immunocompromised host. Sem Respir Infect 1995;10:224-231.

IBMTR/ABMTR MEMBER PROFILE: Richard E. Champlin, MD
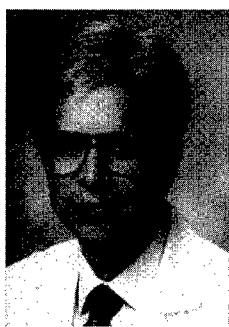
Richard E. Champlin, MD is Professor of Medicine and Chairman of the Department of Hematology at the University of Texas M.D. Anderson Cancer Center in Houston, where he is also Chief, Section of Blood and Bone Marrow Transplantation. He is a fellow of the American College of Physicians, and a member of the American Society of Hematology, and the American Society for Clinical Oncology. Dr. Champlin was the first President of the Council of Donor Transplant and Collection Centers of the National Marrow Donor Program, appointed Chairman, Bone Marrow Transplant Committee of the National Cancer Center Network in 1995 and serves as Chairman of the Scientific Affairs Committee of the American Society of Blood and Marrow Transplantation.

Dr. Champlin has been associated with the International Bone Marrow Transplant Registry (IBMTR) for many years and serves on the IBMTR's Executive Committee and Scientific Advisory Committee. He also serves on the Executive Committee and Scientific Advisory Committee of the Autologous Blood and Marrow Transplant Registry (ABMTR).

An international expert in leukemia and bone marrow transplantation, he is Chair of the IBMTR's Histocompatibility, Alternative Donors, and Stem Cell Sources Working Committee and co-chair of the Chronic Lymphocytic Leukemia Working Committee, a joint scientific committee of the IBMTR and ABMTR.

IBMTR CELEBRATES SILVER ANNIVERSARY

In its 25th year of existence as a productive scientific organization, the International Bone Marrow Transplant Registry (IBMTR) took time out on September 13th for its silver Anniversary Celebration, "Sharing Knowledge - Sharing Hope." Commemorative events included a scientific symposium at the Medical College of Wisconsin attended by more than 200 members of the Milwaukee area transplant and oncology community, Registry founders, Executive and Advisory Committee members, and international representatives from many participating teams.

Speakers included Irving Weissman (Stanford University School of Medicine, Palo Alto, California) speaking on the biology of the hematopoietic stem cell, Mary Horowitz (Medical College of Wisconsin, Milwaukee) speaking on alternative stem cell sources, Malcolm Brenner (St. Jude's Children's Research Hospital, Memphis, Tennessee) speaking on gene therapy, and Megan Sykes (Harvard Medical School, Boston, Massachusetts) speaking on xenotransplantation. Perspectives on the history of the IBMTR and the field of transplantation and a vision for the future were shared by three of the Registry's founding members, Dr. Robert Good of All Children's Hospital, St. Petersburg, Florida; Professor Georges Mathé of the Institut de Cancerologie et d'Immunologie, Villejuif, France; and Dr. George W. Santos of The John Hopkins University School of Medicine, Baltimore, Maryland.

The symposium was followed by a spectacular gala dinner at the Milwaukee Art Museum on Saturday evening, attended by almost 300 Registry friends and supporters. A video presentation, sponsored and produced by Rockwell Automation Allen-Bradley Company of Milwaukee, a founding supporter of the Registry, provided a moving perspective on the Registry's history, and the importance of its work to patients. Dan Rutz, Managing Editor for CNN Health and Medical News, and Mrs. Sue Ann Thompson, First Lady of the State of Wisconsin and a cancer survivor, gave thought-provoking commentaries on cancer care.

Most importantly, the program honored the thousands of transplant recipients and their families. They have, by participating in clinical research and sharing their information with the medical community, played the most important role in the progress made over the past 25 years. Some of these patients were present to share in the Anniversary Dinner. Others had their stories told through a photograph display developed by local artists and premiered at the event. This exhibit will be displayed throughout Southeast Wisconsin and at international scientific meetings.

Our heartfelt thanks go out to the many sponsors and supporters whose generosity and participation made the 25th Anniversary Celebration of the IBMTR a memorable occasion and to all whose contributions have made the past 25 years of scientific work possible.

The International Bone Marrow Transplant Registry (IBMTR) celebrated its 25th anniversary September 13, 1997 with an educational symposium, featuring nationally and internationally known cancer researchers, followed by a gala dinner.

(Photo) Mary M. Horowitz, MD, MS, Scientific Director of the IBMTR, poses with IBMTR founders: (left to right) Robert L. Truitt, PhD, Professor of Pediatrics, Medical College of Wisconsin; George W. Santos, MD, The Johns Hopkins University School of Medicine, Baltimore, MD; Prof. Georges Mathé, Institut de Cancerologie et d'Immunologie, Paris; Robert A. Good, MD, PhD, All Children's Hospital, St. Petersburg, FL; and Robert Peter Gale, MD, PhD, chair of the IBMTR Scientific Advisory Committee and Bone Marrow and Stem Cell Transplant Director, Salick Health Care, Los Angeles.

IBMTR Founder: Alfred A. Rimm, PhD

An article in our 25th Anniversary Newsletter reviewed the history of the IBMTR and ABMTR. However, in my column I amazingly (and embarrassingly) failed to cite contributions of one of the Registry's founders: Alfred A. Rimm. In retrospect I understand why: Al was such a central figure in the IBMTR/ABMTR for so long he became part of the Registry's identity. Mort Bortin never considered Al a "founder"; he *was* the Registry.

Al entered the bone marrow transplant world as Mort's statistical collaborator in murine transplant studies. Their early studies dealt with issues like radiation chimeras, graft-vs-host disease, graft-vs-leukemia and the like. Re-reading these articles today, I am amazed how the central issues Mort and Al raised are the focus of current research. I am also reluctant to try to quantify progress in understanding some issues Mort and Al identified in 1970 (I am referring to substance rather than techniques).

Al volunteered to help Mort with statistical analyses of the early ACS/NIH Bone Marrow Transplant Registry. He also helped bring Mort and his collaborators from Mount Sinai Hospital in Milwaukee to the Medical College of Wisconsin (the current site of the Statistical Center). The first IBMTR/ABMTR-related publication I found by Al is from 1972 making this year the 25th anniversary of Al's involvement with us. This publication was followed by almost 75 more in which Al and his colleagues provided statistical support for IBMTR/ABMTR analyses.

Al's contributions to our organization are too numerous to list. I am especially grateful for three: (1) introducing us to new, innovative techniques for statistical analyses, (2) input to our grant submissions, and (3) recruiting Mary Horowitz. Statisticians are, on average (or perhaps modally), odd. But not Al: doesn't everyone survive weeks on champagne and apples? And I suppose most folks have 4-sided reversible Scotch plaid ties (something to do with kabalah?).

Al left the Medical College of Wisconsin in 1993 to head the Department of Epidemiology and Biostatistics at Case Western Reserve University. Their gain is our loss.

-- *Robert Peter Gale, MD, PhD*
IBMTR Scientific Advisory
Committee Chair

FOUNDATION AND CORPORATE SUPPORT OF THE IBMTR / ABMTR

By
Susan Ladwig, MA
Associate Director
of Development,
Statistical Center

All of us at the IBMTR/ABMTR Statistical Center thank the many contributors who have joined our international collaboration for research in blood and marrow transplantation. Private support for the Registries continues to be vitally important since federal grants cover only 60 percent of the Statistical Center's budget. We gratefully acknowledge the support of the Medical College of Wisconsin; the National Cancer Institute; the National Institute of Allergy and Infectious Disease; the National Heart, Lung and Blood Institute; the Department of Defense; and the generosity of the following foundations and corporations:

Non-Federal Support Listing for the IBMTR / ABMTR
(Grant Awards Since 1995)

Aastrom Biosciences
Activated Cell Therapy, Inc.
* Alpha Therapeutic Corporation
Alpha Therapeutic GmbH
* American Oncology Resources
* Amgen, Inc.
Amgen Europe AG
Anonymous
Astra Arcus AB
* Astra USA
* Baxter Healthcare Corporation
* Bayer Corporation
Biochem Pharma
Biogen
BioWhittaker, Inc.
BIS Laboratories
* Blue Cross and Blue Shield
    Association
The Lynde and Harry Bradley
    Foundation
* Bristol-Myers Squibb Company
Cell Therapeutics, Inc.
* CellPro, Inc.
* Centeon
Center for Advanced Studies in
    Leukemia
* Chimeric Therapies, Inc.
* Chiron Therapeutics
Cigna Health Care
* COBE BCT Inc.
* Coram Healthcare
Coulter Corporation
Charles E. Culpeper Foundation
Eleanor Naylor Dana Charitable
    Trust

Deborah J. Dearholt Memorial Fund
The Eppley Foundation for Research
ESSEX Pharma GmbH (Germany)
Fujisawa USA
Genentech, Inc.
Glaxo Wellcome, Inc.
Hewlett-Packard Company
Hoechst Marion Roussel, Inc.
* ICN Pharmaceuticals, Inc.
* Immunex Corporation
* Janssen Pharmaceutica
The Kettering Family Foundation
Kirin Brewery Company (Japan)
Robert J. Kleberg, Jr. & Helen C.
    Kleberg Foundation
Herbert H. Kohl Charities
Lederle International
Life Technologies, Inc.
* The Liposome Company
Nada and Herbert P. Mahler
    Charities
* MDS Nordion
Medical SafeTEC
* MGI Pharma, Inc.
* Milliman & Robertson, Inc.
Milstein Family Foundation
The Milwaukee Foundation/
    Elsa Schoeneich Medical
    Research Fund
NCGS and Associates, Inc.
NeXstar Pharmaceuticals, Inc.
Samuel Roberts Noble Foundation

Corporate Member

Northwestern Mutual Life
    Insurance Company Foundation
Novartis Pharmaceuticals, Inc.
* Ortho Biotech Inc.
John Oster Family Foundation
Jane & Lloyd Pettit Foundation
Alirio Pfiffer Bone Marrow
    Transplantation Support
    Association (Brazil)
* Pfizer Inc.
Pharmacia and Upjohn
* Principal Mutual Life Insurance
    Company
QLT PhotoTherapeutics, Inc.
Quantum Health Resources
RGK Foundation
Roche Laboratories
Rockwell Automation/Allen-
    Bradley Co.
RPR Gencell
* SangStat Medical Corporation
Schering-Plough International
Walter Schroeder Foundation, Inc.
* Searle
SEQUUS Pharmaceuticals
Stackner Family Foundation
The Starr Foundation
Joan and Jack Stein Foundation
StemCell Technologies Inc
SyStemix
Therakos
TS Scientific and Planer Products
Laboratories Wyeth France
* Wyeth-Ayerst Laboratories
Xoma Corporation

A Special
Thank You
to our
1998 Annual
IBMTR / ABMTR
Meeting Supporters

AASTROM BIOSCIENCES
AMGEN, INC.
BAXTER HEALTHCARE, INC.
    BIOTECH GROUP
BIOCHEM PHARMA
BIS LABORATORIES
BRISTOL-MYERS SQUIBB
    ONCOLOGY
CELL THERAPEUTICS, INC.
CELLPRO, INC.
CENTEON
CHIRON THERAPEUTICS, INC.
COBE BCT
FUJISAWA USA
ICN PHARMACEUTICALS,
    INC.
IMMUNEX CORPORATION
ISHAGE
THE LIPOSOME COMPANY,
    INC.
MEDICAL SAFETEC
MEDIMMUNE, INC.
NEXSTAR PHARMACEUTICALS
NOVARTIS PHARMACEUTICALS
ORTHO BIOTECH INC.
PFIZER INC.
PHARMACIA & UPJOHN
ROCHE LABORATORIES
SANGSTAT MEDICAL
    CORPORATION
SCHERING-PLOUGH
    CORPORATION
SEARLE
SEQUUS
PHARMACEUTICALS, INC.
STEMCELL TECHNOLOGIES
    INC
SYSTEMIX
THERAKOS
WYETH-AYERST
    LABORATORIES

IBMTR / ABMTR CORPORATE MEMBERSHIP PROGRAM

Several corporations have joined the IBMTR/ABMTR Corporate Membership Program (see above). The annual membership program provides member organizations with informational materials on blood and bone marrow transplantation developed by the IBMTR/ABMTR Information Resource Service.

The program includes subscriptions to the *Statistical Center Report on Survival Statistics for Blood and Marrow Transplants*, *IBMTR and ABMTR Newsletters*, the worldwide *IBMTR/ABMTR Directory of Blood and Marrow Transplant Teams*, and the *IBMTR/ABMTR Summary Slides on State-of-the-Art in Blood and Marrow Transplantation* as well as invitations to our meetings and educational forums and access to the IBMTR/ABMTR databases for simple analyses. These resources are useful for marketing managers, medical directors, research directors, product managers, case managers or transplant coordinators.

For additional information on the Corporate Membership Program, please contact Susan Ladwig, Associate Director of Development ☎ (414) 456-8363, Fax: (414) 456-6530.

ABMTR Advisory Committee

IBM**R**

The IBMTR/ABMTR Statistical Center introduces a new logo. The new look reflects the cooperation between the IBMTR & ABMTR and our optimism for continuing progress in blood and marrow transplantation.

Contents:

The ABMTR Newsletter is funded by an educational grant from Bristol-Myers Oncology.

MEDICAL COLLEGE OF WISCONSIN

ABMTR INITIATES STUDY OF AUTOTRANSPLANTS FOR ADVANCED OVARIAN CANCER

By Patrick J. Stiff, MD
Loyola University Medical Center, Maywood, Illinois

Despite recent improvements in conventional therapy of advanced ovarian carcinoma, the mortality rate remains 65% at 5 years and few women are cured[1-4]. Although initial response rates are high, drug resistance develops rapidly. Response rates with conventional salvage therapy are only 10-40% with responses lasting an average of 6 months.

Dose Intensity and Ovarian Cancer
Considerable data on dose-intensity in ovarian cancer treatment suggest that high-dose therapy may improve outcome[5-7]. *In vitro* studies demonstrate a favorable dose-response relationship for platinum, other alkylating agents and mitoxantrone, and additive or synergistic cytotoxicity with drug combinations[8-12]. Early transplant trials indicate that intensifying

platinum-based chemotherapy to doses to approximately 5 times conventional levels increases response rates[13-15]. Patterns of response appear similar to those observed with high-dose therapy for lymphoma, testicular cancer and, possibly, breast cancer.

Relapsed/Refractory Ovarian Cancer
Early autotransplant trials usually included patients failing 2 prior regimens, with platinum-resistance (tumor progression during or within 6 months of achieving remission with platinum-based therapy). Responses varied from 55-75%, with substantial numbers of clinical complete remissions. Remission durations were short, usually 5-7 months. However, 10-15% of women had long-term remissions suggesting the possibility of cure.

SPECIAL ISSUE
REPORT ON STATE OF THE ART IN BLOOD AND MARROW TRANSPLANTATION
WITH GUIDE TO IBMTR/ABMTR SUMMARY SLIDES
(see pages 6-12)

SCIENCE, SUNSHINE AND SCOTTSDALE ON THE AGENDA FOR 1997 ANNUAL IBMTR/ABMTR PARTICIPANTS' MEETING

By D'Etta Waldoch Koser, CMP, Associate Director, International Programs, IBMTR/ABMTR

The IBMTR/ABMTR Annual Meeting is scheduled for February 22-25 at the Radisson Resort Scottsdale. A full program of Scientific Sessions addressing the basic and clinical science of blood and marrow transplantation, Working Committee meetings and Data Management training is planned. CME credits are available.

♦ **Deadline for abstract submission extended to December 15.** Abstract Forms are available through the Statistical Center. $500 will be awarded to the abstract using the most innovative techniques for clinical research, with special attention given to studies benefitting from
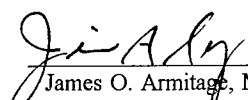
use of Registry data. Poster Sessions will be combined with a light dinner buffet each evening.

♦ **Housing is limited**; fax your Room Reservation Form to the Radisson Resort Scottsdale *today* to take advantage of special discounted guest room rates during peak season.

♦ Watch for "Provisional Program Update." Enclosed in that mailing are Northwest Airlines "Association Dollars Off Certificates" for discounted airfares for IBMTR/ABMTR meeting participants (some restrictions apply).

James O. Armitage, MD,
Chair, Scientific Advisory
Committee

New ABMTR Studies Evaluate Growing Use of Autologous Transplantation

The Autologous Blood & Marrow Transplant Registry – North America (ABMTR) continues to grow. Currently, 188 participating centers in the United States, Canada, Mexico and South America provide data to the Registry. More than 100 physicians from these centers volunteer their time to serve on one or more ABMTR Working Committees, to plan and conduct studies using these data.

ABMTR centers registered about 7,000 new patients in 1995. The total number of transplants available for study exceeds 23,000. The distribution of diseases treated by those transplants is shown below.

Approximately two-thirds of transplants were for lymphoma (Hodgkin or non-Hodgkin) or breast cancer. However, more than 400 transplants each for neuroblastoma, ovarian cancer and testicular cancer were registered. Additionally, over 2,000 transplants for acute leukemia and over 1,000 for multiple myeloma are available for study. The Registry provides a unique resource for studying the impact of this complicated therapy on the management of patients with these disorders.

This issue of the *Newsletter* focuses on research being done in the use of high-dose therapy and transplantation to manage patients with ovarian cancer. However, this is just one of numerous ongoing studies that are possible only because of the participation of physicians and their transplant teams.

On behalf of the Registry, I want to express thanks to all those whose efforts are making this project a success.

ABMTR Advisory Committee Chair, James O. Armitage, MD, is Professor and Chairman, Department of Medicine, University of Nebraska Medical Center, Omaha. Dr. Armitage is also current President of the American Society for Clinical Oncology.

Distribution of autotransplants performed beween 1989 and 1995, registered with the ABMTR by 188 centers in North and South America

Disease	Numbers, %
Breast cancer	7646 (33)
Non-Hodgkin lymphoma	5789 (25)
Hodgkin lymphoma	2992 (13)
Acute myelogenous leukemia	1965 (9)
Acute lymphoblastic leukemia	511 (2)
Chronic myelogenous leukemia	205 (1)
Multiple myeloma	1192 (5)
Neuroblastoma	579 (3)
Ovarian cancer	440 (2)
Testicular cancer	406 (2)
Brain tumor	272 (1)
Lung cancer	129 (<1)
Bone sarcoma	118 (<1)
Other cancer	813 (3)
Total	23,057

Five IBMTR/ABMTR Studies to be Presented at the American Society of Hematology Meetings in December

Message from the Scientific Director

The IBMTR/ABMTR Statistical Center is coordinating more than 50 transplant-related studies, addressing a wide range of issues. Current projects include comparison of unrelated donor and autologous transplants for leukemia, determining risk factors for second cancers after allogeneic and autologous transplants, and identifying prognostic factors in autotransplants for breast cancer, among many others. These studies are possible because of data contributed by hundreds of transplant centers, 20 years of statistical expertise in analyzing transplant data and active involvement of investigators from IBMTR and ABMTR institutions.

IBMTR/ABMTR studies to be presented at the annual meeting of the American Society of Hematology (ASH), December 6-10, 1996 include:

Effect of Prior Interferon Therapy on Outcome of HLA-Identical Sibling Bone Marrow Transplant for Chronic Myelogenous Leukemia (CML) in First Chronic Phase; to be presented by Mary M. Horowitz (platform session). This study of 882 transplants for CML indicates that treatment with α-interferon pretransplant does not adversely affect outcome of HLA-identical sibling transplants. Analysis of additional data regarding pretransplant interferon dose and response is in progress and will be available in early December.

Solid Cancers after Bone Marrow Transplantation; to be presented by Rochelle E. Curtis (platform session). This study was done in collaboration with the Fred Hutchinson Cancer Center and the Radiation Epidemiology Branch of the National Cancer Institute. It found that bone marrow transplant recipients have an increased risk of developing solid cancers at specific sites. A trend toward increasing risk with time posttransplant as well as greater risk among younger patients underscores the need for lifelong surveillance of transplant recipients.

Long-term Survival and Analysis of Late Causes of Death after Allogeneic Bone Marrow Transplantation; to be presented by Gérard Socié (platform session). Patient, disease, and transplant characteristics were analyzed for their association with late death in 5,773 patients alive and disease-free ≥ 2 years posttransplant. The data suggest that graft-versus-host disease (GVHD) and relapse contribute to late as well as early posttransplant mortality and suggest the need for long-term follow-up of transplant recipients.

Effects of G- and GM-CSF on Outcomes Following HLA-Identical Sibling Bone Marrow Transplants for Early Leukemia; to be presented by Kerry Atkinson (poster session). The study analyzed patients receiving HLA-identical sibling bone marrow transplants for acute leukemia in complete remission and CML in first chronic phase. Preliminary analysis comparing patients receiving G- or GM-CSF with patients not receiving growth factors showed shorter time to neutrophil recovery with growth factors. There was no increase in relapse risk in any disease. Acute GVHD was not increased but there was increased risk of chronic GVHD in older patients receiving G- or GM-CSF.

A Decision Analysis of Unrelated Donor Transplantation for CML; to be presented by Stephanie J. Lee (platform session). This study uses data from the IBMTR and the National Marrow Donor Program, analyzed by Dr. Stephanie Lee (Dana-Farber Cancer Institute, Boston). Timing of unrelated transplants for CML in chronic phase was studied using a Markov model, incorporating the competing risks of death from CML and bone marrow transplantation, risks of chronic GVHD and adjustments for quality of life posttransplant and risk aversion. The study found a benefit of <u>early</u> transplantation that was greatest for younger persons, but evident even for patients >40 years of age.

An important new area of study for the ABMTR is highlighted in this *Newsletter*: autotransplants for ovarian cancer. Patrick Stiff, Chair of the Ovarian Working Committee, reviews recent studies suggesting a role for high-dose therapy in advanced ovarian cancer (cover story). A short questionnaire was recently distributed to obtain additional data on women with ovarian cancer registered with the ABMTR. This study will provide important information on posttransplant outcomes and prognostic factors in a large number of women. We urge your participation.

Another important function of the Statistical Center is to provide yearly overviews of transplant outcomes. This issue of the *Newsletter* provides an interpretation guide for our **1996 Summary Slides on State-of-the-Art in Blood and Marrow Transplantation.** The slides will be sent to all IBMTR/ABMTR Participating Teams and to IBMTR/ABMTR Corporate Members in January.

Thank you for your participation in the research programs of the IBMTR and ABMTR. With your collaboration, we are able to continue our important work to improve the success of blood and marrow transplantation.

Mary M. Horowitz,
MD, MS
Scientific Director

Mary M. Horowitz, MD, MS is Scientific Director of the IBMTR/ABMTR and Professor of Medicine at the Medical College of Wisconsin

A survey of U.S. programs with active autotransplant protocols for ovarian carcinoma was conducted in 1992[16]. Eleven centers reported 153 patients of whom 146 received transplants for relapsed or refractory disease. Among 61 women with platinum-resistant tumors, 51% had partial and 34%, complete responses. Among 37 with platinum-sensitive disease, 14% had partial and 73%, complete responses. Median progression free survival (PFS) in the entire group was 6 months. 14% of women were disease-free 1 year after treatment.

A trial at Loyola University (Chicago) also found an association between platinum-sensitivity and transplant outcome[17]. Among 30 women receiving high-dose mitoxantrone, carboplatinum and cyclophosphamide, median PFS was 10.1 months for 10 with platinum-sensitive disease versus 5.1 months for 20 with platinum-resistance (p=.03). 80% of those with platinum-sensitive disease were alive 18 months posttransplant. A recent (unpublished) update of 34 patients with platinum-sensitive disease <1 cm in diameter at time of transplant showed median PFS of 19 months and overall survival of 30 months. These data, when compared to historical results in relapsed ovarian cancer, suggest that autotransplants may be superior to conventional therapy for patients with platinum-sensitive tumors, though one must be cautious in interpreting single-arm studies of patients referred for transplant.

Persistent Disease at Second-Look Laparotomy

Several pilot studies of autotransplants in women with persistent ovarian cancer at second-look laparotomy are reported. Dauplat et al. described 14 such patients (12 with microscopic disease) receiving a single course of high-dose melphalan[18]. Three-year PFS and survival were 33% and 64%. A recently published update demonstrated median PFS of 27 months in 31 women[19]. Of 19 women reported by Viens et al., 3 of 10 with disease <2 cm in diameter and 6 of 9 with pathologic complete remissions were alive and disease-free at a median follow-up of 22 months after high-dose therapy[20]. Among 87 women receiving autotransplants after second-look laparotomy reported by Extra et al., median survival after transplant was 47 months[21]. Sixty-five (76%) of these had suboptimal stage III and IV disease, a group with, historically, only about 2 years

survival after conventional-dose platinum and cyclophosphamide. These data suggested better response with auto-transplants and also demonstrated its safety. The fatal toxicity rate was only 1.1%.

The Southwest Oncology Group is currently conducting a randomized trial comparing two transplant regimens for patients with <3 cm disease at second-look laparotomy to verify safety and efficacy of auto-transplants in this setting.

Initial Management of Ovarian Cancer

Several studies report results of high-dose chemotherapy after induction chemotherapy for advanced ovarian cancer. Benedetti-Panici et al. treated 35 women presenting with Stage III or IV disease with

---

To facilitate the ABMTR study of ovarian cancer, a request for additional data was recently sent to participating transplant centers. We encourage you to submit this brief supplemental form as quickly as possible. Additionally, a new form is being developed to prospectively capture data on autotransplants for ovarian cancer. Analyses of these data will be important for designing future clinical trials and improving outcome of transplants for ovarian cancer.

2-4 cycles of standard chemotherapy followed by either high-dose cisplatinum, carboplatinum and etoposide or carboplatinum, etoposide and melphalan stem cell rescue[22]. Among 24 women completing all therapy, 10 (42%) had a pathologic complete response. Seven remain in remission more than 3 years posttransplant.

Fennelly et al. treated 16 patients (10 suboptimally debulked) with high-dose cyclophosphamide and Taxol with cytokine support only for 2 cycles followed by 4 courses of carboplatinum and cyclophosphamide and blood stem cell rescue[23]. Five (38%) women had a negative second-look laparotomy. This may or may not be better than achievable with Taxol and cisplatinum at conventional doses.

The Next Step

While these data are encouraging, the true role of autotransplants in management of advanced ovarian cancer is still uncertain. Randomized trials are needed. Under the auspices of the National Cancer Institute (NCI), one such trial will soon start in the U.S. Cooperative Groups (GOG164). In this study, after initial surgery, women with Stage III ovarian cancer will receive 4-6 cycles of a platinum-based regimen followed by second-look laparotomy. Those with low tumor burden (microscopic disease for optimal Stage III, <1 cm for suboptimal Stage III) will be randomized to either six cycles of carboplatin and Taxol or a single cycle of high-dose carboplatin, mitoxantrone and cyclophosphamide[17] and a blood stem cell transplant.

Role of the ABMTR

Little is known about which patients are most likely to benefit from high-dose therapy. The influence of timing, platinum-sensitivity, tumor bulk, histology and grade, high-dose chemotherapy regimen, and multiple cycles of moderate-dose chemotherapy are all important issues. Neither the currently planned randomized nor single institution Phase II trials can address all of these satisfactorily. The ABMTR, by accumulating data on hundreds of autotransplants for ovarian cancer, is uniquely suited to these issues. **Thanks to a generous educational grant from Amgen, Inc., an ABMTR study of autotransplants for ovarian cancer was recently initiated.** This study will define the survival rate after autotransplants in a large group of women, identify prognostic factors for transplant outcome and suggest the most successful transplant strategies.

To facilitate the ABMTR study of ovarian cancer, a request for additional data was recently sent to participating transplant centers. We encourage you to submit this brief supplemental form as quickly as possible. Additionally, a new form is being developed to prospectively capture data on autotransplants for ovarian cancer. Analyses of these data will be important for designing future clinical trials and improving outcome of autotransplants for ovarian cancer.

REFERENCES

1. Ozols RF, Young RC. Chemotherapy of ovarian cancer. Semin Oncol **18**: 222-232, 1991.
2. Runowicz CD. Advances in the screening

and treatment of ovarian cancer. CA **42**: 327-349, 1992.

3. Alberts DS, Green SG, Hannigan EV, et al. Improved therapeutic index of carboplatin plus cyclophosphamide versus cisplatin plus cyclophosphamide: Final report by the Southwest Oncology Group of a phase III randomized trial in stage III and IV ovarian cancer. J Clin Oncol **10**: 706-717, 1992.

4. McGuire WP, Hoskins WJ, Brady MF, et al. A phase III trial comparing cisplatin/cytoxan and cisplatin/taxol in advanced ovarian cancer. Proc Am Soc Clin Oncol **12**: 255 (abstract no. 808), 1993.

5. Levin L, Hryniuk WM. Dose intensity analysis of chemotherapy regimens in ovarian cancer. J Clin Oncol **5**: 756-760, 1987.

6. Levin L, Simon R, Hryniuk W. Importance of multiagent chemotherapy regimens in ovarian carcinoma: dose intensity analysis. J Natl Cancer Inst **85**: 1732-42,1993.

7. Ozols RF, Thigpen JT, Dauplat J, et al. Advanced ovarian cancer. Dose intensity. Ann Oncol **4** (Suppl 4): S49-56, 1993.

8. Alberts DS, Young L, Mason N, Salmon SE. In vitro evaluation of anticancer drugs against ovarian cancer at concentrations achievable by intraperitoneal administration. Semin Oncol **12** (Suppl 4): 38-42, 1985.

9. Lidor Y, Shpall EJ, Peters WP, Bast RC Jr. Alkylating agents and immunotoxins exert synergistic activity against ovarian cancer cell lines. Proc Am Assoc Cancer Res **30**: 401 (abstract no. 1593), 1989.

10. Beherns BC, Hamilton TC, Masuda H, et al. Characterization of a cis-diamine dichloro-platinum (II)-resistant human ovarian cancer cell line and its use in evaluation of platinum analogs. Cancer Res **47**: 414-418,1987.

11. Teicher B, Holden SA, Jones SM, Eder JP, Herman TS. Influence of scheduling in two-day combinations of alkylating agents in vivo. Cancer Chemother Pharmacol **25**: 161-166, 1989.

12. Lidor YJ, Shpall EJ, Peters WP, Bast RC. Synergistic cytotoxicity of different alkylating agents for epithelial ovarian cancer. Int J Cancer **49**: 704-707, 1991.

13. Mulder POM, Sleijfer DT, Willemse PHB, deVries EGE, Mulder NH. High-dose cyclophosphamide or melphalan with escalating doses of mitoxantrone and autologous bone marrow transplantation for refractory solid tumors. Cancer Res **49**, 4654-4658, 1989.

14. Shea TC, Flaherty M, Elias A, et al. A phase I clinical and pharmacokinetic study of carboplatin and autologous bone marrow support. J Clin Oncol **7**: 651-661, 1989.

15. Shpall EJ, Clark-Pearson D, Soper JT, et al. High dose alkylating agent chemotherapy with autologous bone marrow support in patients with stage III/IV epithelial ovarian cancer. Gynecol Oncol **38**: 386-391, 1990.

16. Stiff P, Antman K, Broun ER, et al. Bone marrow transplantation for ovarian carcinoma in the United States: A survey of active programs. In: Dicke KA and Keating A (ed.) Proceed Sixth International ABMT Symposium. Cancer Treatment Research Education Fund; Arlington, pp 192-198, 1993.

17. Stiff P, Bayer R, Camarda M, et al. A phase II trial of high dose mitoxantrone, carboplatin, and cyclophosphamide with autologous bone marrow rescue for recurrent epithelial ovarian carcinoma: Analysis of risk factors for clinical outcome.

Gynecol Oncol **57**: 278-285, 1995.

18. Dauplat J, Legros M, Condat P, et al. High dose melphalan and autologous bone marrow support for treatment of ovarian carcinoma with positive second-look operation. Gynecol Oncol **34**: 294-298, 1989.

19. Legros M, Fluery J, Cure H, et al. High dose chemotherapy (HDC) and autologous bone marrow transplant (ABMT) in 31 advanced ovarian cancers: Long term results. Proc Am Soc Clin Oncol **11**: 222 (abstract no. 700), 1992.

20. Viens P, Maraninchi D, Legros M, et al. High dose melphalan and autologous marrow rescue in advanced epithelial ovarian carcinomas: A retrospective analysis of 35 patients treated in France. Bone Marrow Transplant **5**: 227-233, 1990.

21. Extra JM, Giacchetti S, Bourstyn, et al. High dose chemotherapy with autologous bone marrow reinfusion as consolidation therapy for patients with advanced ovarian adenocarcinoma. Proc Am Soc Clin Oncol **11**: 234 (abstract no. 749), 1992.

22. Benedetti-Painica P, Greggi S, Scambia G, et al. Very high dose chemotherapy (VHDC) with autologous peripheral stem cell (APSC) as hematologic support (HS) in previously untreated advanced ovarian cancer (AOC). Proceed Soc Gyn Onc, p. 30, (abstract no. 73), 1995.

23. Fennelly D, Schneider J, Bengala C, et al. Escalating-dose taxol plus high-dose (HD) cyclophosphamide plus G-CSF followed by rapidly sequenced courses of high-dose carboplatin plus Cyclophosphamide rescued with peripheral blood progenitor cells in patients with stage IIC-IV ovarian cancer. Gynecol Oncol **56**: 121 (abstract no. 45), 1995.

ABMTR MEMBER PROFILE: PATRICK J. STIFF, MD

Patrick J. Stiff, MD is Associate Professor of Medicine and Director of the Bone Marrow Transplant Program at the Loyola University Stritch School of Medicine in Maywood, Illinois. Dr. Stiff is a member of the ABMTR Scientific Advisory Committee and chair of the Ovarian Cancer Committee. He is nationally recognized for his pioneering work in autotransplants for ovarian cancer.

After receiving his medical degree in 1975 from Loyola University, Dr. Stiff completed a fellowship in medical oncology at Memorial Sloan-Kettering Cancer Center in New York. In 1981, he was appointed Assistant Professor and Director of Bone Marrow Transplantation Services at Southern Illinois University School of Medicine in Springfield, Illinois where he was named Faculty Member of the Year in 1985. He joined the Department of Hematology/Oncology at Loyola in 1986.

Dr. Stiff is a member of many scientific and medical organizations. Among these are the Gynecologic Oncology Executive Committee, Leukemia Committee and Lymphoma Committee of the Southwest Oncology Group and Board of Directors of the International Society for Hematotherapy and Graft Engineering. Dr. Stiff is also a member of the State of Illinois Medical Advisory Committee, serving on the Subcommittee on Transplantation. Dr. Stiff has authored or co-authored over 30 articles in scientific journals as well as many book chapters.

Through Dr. Stiff's efforts the ABMTR has developed a data collection form for ovarian cancer and initiated the first ABMTR analysis of autotransplants in ovarian cancer.

1996 SUMMARY SLIDES SHOW CURRENT USE AND OUTCOME OF BLOOD AND MARROW TRANSPLANTATION

By Philip A. Rowlings, MD, MS, IBMTR/ABMTR Assistant Scientific Director

Since 1972 the IBMTR has collected data from over 300 transplant centers, worldwide. The IBMTR database includes information for about 40% of allogeneic bone marrow transplants done between 1970 and 1995. In 1991, the ABMTR began collecting data on autotransplants from centers in North and South America. More than 180 autotransplant centers now contribute data to the ABMTR. The ABMTR database includes information for about 50% of autotransplants done in North America between 1989 and 1995.

Using these data, the Statistical Center periodically prepares and distributes slides summarizing current use and outcome of allogeneic and autologous hematopoietic stem cell transplants. **This year's Summary Slides, made possible by a generous educational grant from Bristol-Myers Oncology, are described below.**

Slide 1: Use of blood and marrow transplants continues to increase. We estimate 12,000 allogeneic and 18,000 autologous transplants were done in 1995, worldwide.

Slide 2: Most autotransplants use hematopoietic progenitor cells collected from blood. Fewer than 20% are done with bone marrow alone. In contrast, over 90% of allografts use bone marrow. Despite recent interest in collecting allogeneic cells from peripheral blood or umbilical cord blood, few such transplants have yet been done.

Slide 3: Most allogeneic transplants are from HLA-identical sibling donors. However, only about 30% of transplant candidates have such a donor. Increasing availability of HLA-typed volunteers through large national and international registries has enabled increasing use of unrelated donors for bone marrow transplants. Transplants
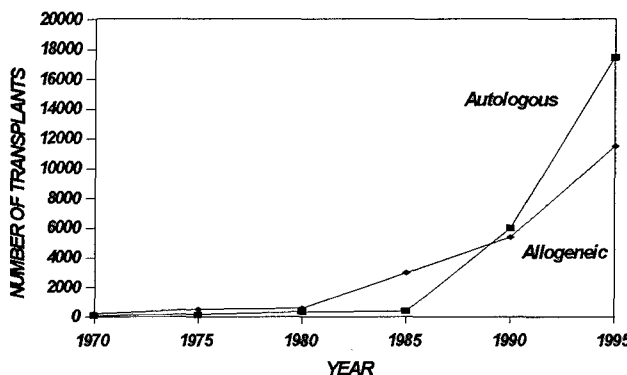
Slide 1. *Annual Number of Blood and Marrow Transplants Worldwide, 1970-1995*
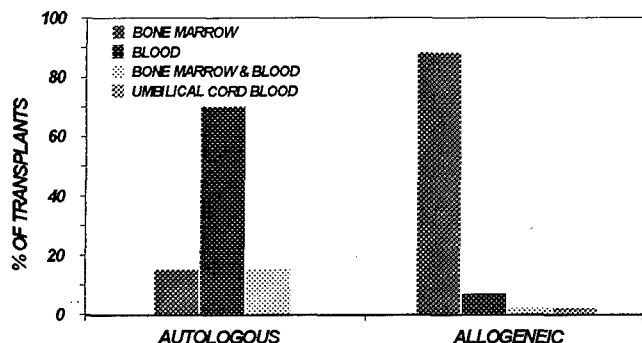
Slide 2. *Stem Cell Sources, 1995*
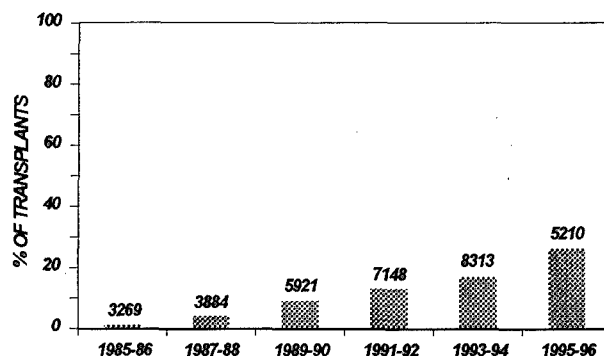
Slide 3. *Percent of Allogeneic Transplants from Unrelated Donors*

from unrelated donors now account for about 25% of allogeneic transplants.

Slide 4: The most common indications for allogeneic and autologous transplants differ. Among cases reported to the IBMTR/ABMTR, 74% of allogeneic transplants are for leukemia or preleukemia: 22% for chronic myelogenous leukemia (CML), 23% for acute myelogenous leukemia (AML), 19% for acute lymphoblastic leukemia (ALL), 7% for myelodysplastic syndromes and 3% for other leukemias. Ten percent are for other cancers including non-Hodgkin lymphoma (6%), multiple myeloma (3%), and Hodgkin disease (<1%). The remainder are for aplastic

anemia (7%), immune deficiencies (2%), inherited disorders of metabolism (1%) and other non-malignant disorders (6%). Autotransplants are used to treat cancer. The most common indications for auto-transplants in North America in 1995 were breast cancer (42%), non-Hodgkin lymphoma (23%), Hodgkin disease (9%), multiple myeloma (8%), AML (6%), ovarian cancer (2%), ALL (1%), CML (1%), with 8% for a variety of other cancers. The most striking recent change in autotransplant use is the dramatic increase in autotransplants for breast cancer. In 1989, about 15% of autotransplants in North America were for breast cancer while in 1995, over 40% were

for breast cancer.

Slide 5: 100-day mortality is often used as a gauge of procedure-related toxicity. Allogeneic transplants are associated with high risks of graft-versus-host disease (GVHD), infections and liver toxicity, resulting in relatively high early mortality. Among HLA-identical transplants done in 1995 and reported to the IBMTR, 100-day mortality rates range from about 10% for persons with acute leukemia in first remission to almost 40% for those with advanced leukemia. Progressive leukemia
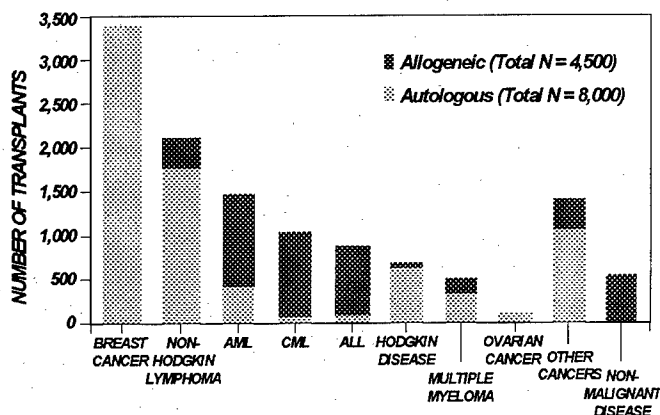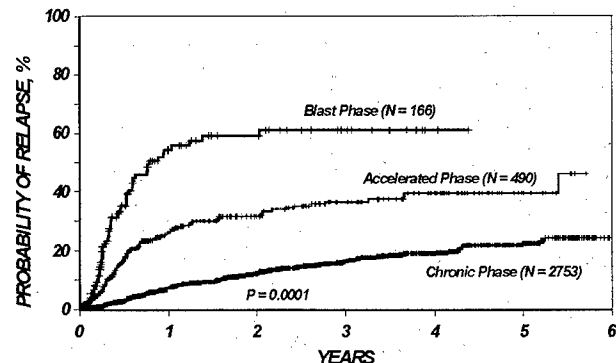
Slide 4. *Indications for Blood and Marrow Transplantation in North America, 1995*
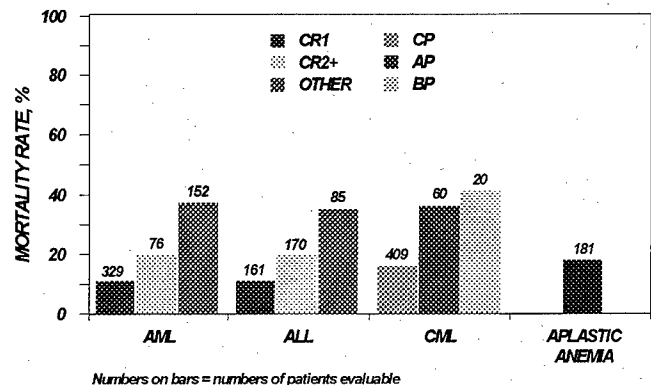
Slide 5. *100-Day Mortality after HLA-identical Sibling Transplants, 1995*
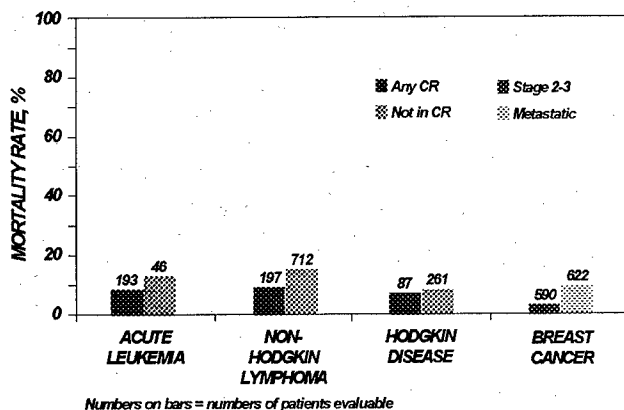
Slide 6. *100-Day Mortality after Autotransplants, 1995*

Slide 7. *Probability of Relapse after HLA-identical Sibling BMT for Chronic Myelogenous Leukemia, 1989-1995*

contributes to the early mortality rates among patients transplanted with advanced disease.

Slide 6: Early mortality is generally lower after auto- than allotransplants. Among autotransplants done in 1995 and reported to the ABMTR, 100-day mortality ranges from <5% in women with Stage 2-3 breast cancer to about 15% in persons with advanced lymphoma.

Slides 7, 8: CML is the most frequent indication for allogeneic bone marrow transplantation. Among 3,409 recipients of HLA-identical sibling transplants done

between 1989 and 1995, reported to the IBMTR, 3-year probabilities of relapse (95% confidence interval) were 16 ± 2% for 2,753 transplants done in first chronic phase, 36 ± 6% for 490 in accelerated phase, and 61 ± 11% for 166 in blast phase. 3-year probabilities of leukemia-free survival (LFS) were 59 ± 2%, 37 ± 5% and 17 ± 7%, respectively.

Slide 9: Persons relapsing after an HLA-identical sibling transplant for CML often survive for long intervals with conventional treatment. Many achieve durable hematologic and cytogenetic remissions with infusion of donor lymphocytes.

Consequently, 3-year survival rates after transplants are somewhat higher than LFS rates: 66 ± 2% in chronic phase, 44 ± 5% in accelerated phase, and 19 ± 7% in blast phase.

Slide 10: Only about 30% of persons with CML have an HLA-identical sibling donor. Unrelated donor transplants can cure CML but are associated with higher risks of GVHD and transplant-related mortality. Additionally, unrelated donor transplants are often delayed because of the time required to identify a donor and reluctance to risk the high transplant-related mortality. Delaying transplantation may adversely
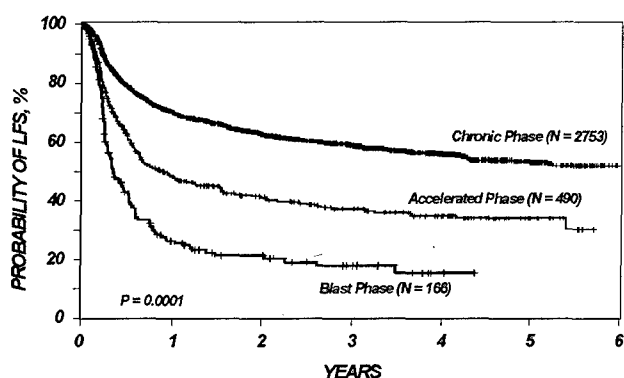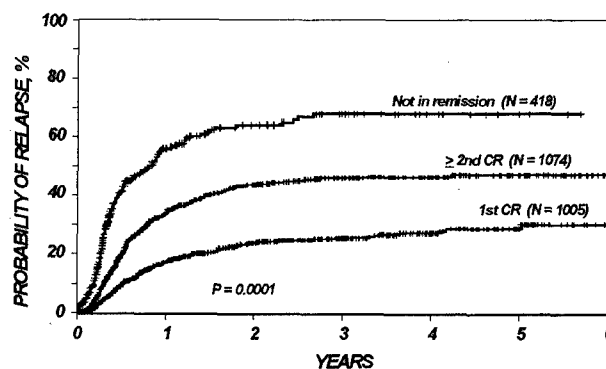

Slide 8. *Probability of Leukemia-free Survival after HLA-identical Sibling BMT for Chronic Myelogenous Leukemia, 1989-1995*
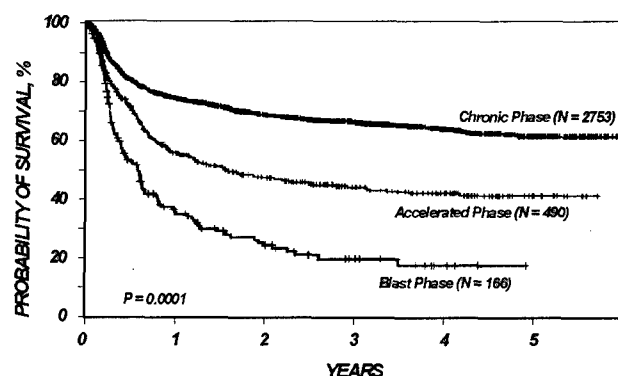
Slide 9. *Probability of Survival after HLA-identical Sibling BMT for Chronic Myelogenous Leukemia, 1989-1995*
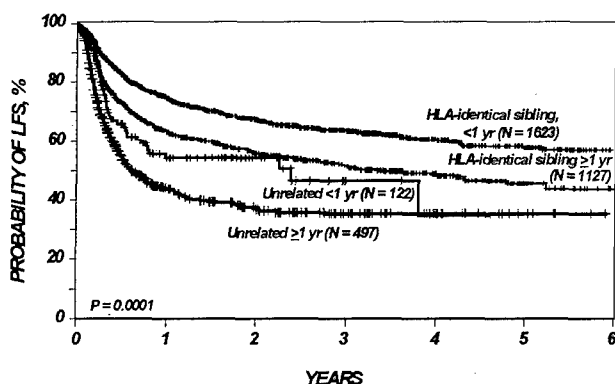
Slide 10. *Probability of LFS after BMT for Chronic Myelogenous Leukemia in Chronic Phase, by Donor Type and Time to Transplant*

Slide 11. *Probability of Relapse after HLA-identical Sibling BMT for Acute Lymphoblastic Leukemia 1989-1995*

affect outcome. Slide 10 shows LFS after 1,623 HLA-identical sibling transplants done <1 year after diagnosis of CML (64 ± 3% at 3 years), 1,127 HLA-identical sibling transplants done a year or more after diagnosis (51 ± 3%), 122 unrelated donor transplants done <1 year after diagnosis (47 ± 13%), and 497 unrelated donor transplants done a year or more after diagnosis (35 ± 5%). Outcome of unrelated donor transplantation may be affected by factors other than interval between diagnosis and transplant such as donor-recipient histocompatibility, recipient age and others.

Slides 11, 12: Most patients with ALL are

cured with conventional chemotherapy. Consequently, bone marrow transplants are generally reserved for patients failing conventional therapy, i.e., in relapse or second or subsequent remission, or patients in first remission with prognostic factors predicting a high risk of failure with conventional therapy. The most frequent indications for transplants in first remission are older age, high leukocyte count at diagnosis, Ph[1] and other chromosome abnormalities and difficulty obtaining a first remission. Among 2,497 recipients of HLA-identical sibling transplants between 1989 and 1995, reported to the IBMTR, 3-year probabilities of relapse were 25 ± 4% for 1,005

transplants done in first remission, 46 ± 4% for 1,074 in second or subsequent remission, and 68 ± 7% for 418 done in relapse. 3-year probabilities of LFS were 54 ± 4%, 40 ± 13% and 20 ± 5%, respectively.

Slides 13, 14: Among 357 recipients of autotransplants for ALL done between 1989 and 1995, reported to the ABMTR, 3-year probabilities of relapse were 49 ± 14% for 102 transplants done in first remission, 70 ± 7% for 228 done in second or subsequent remission, and 76 ± 24% for 27 done in relapse. 3-year probabilities of LFS were 43 ± 12%, 25 ± 6% and 17 ± 17%, respectively.
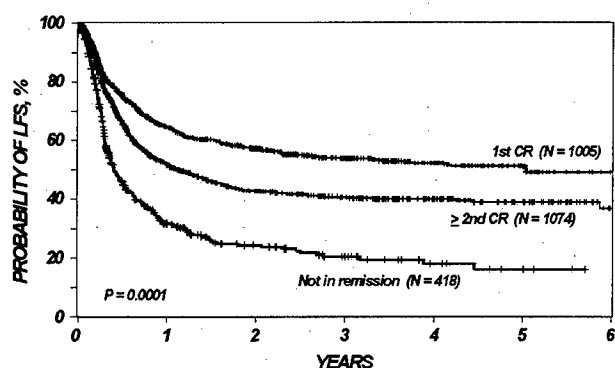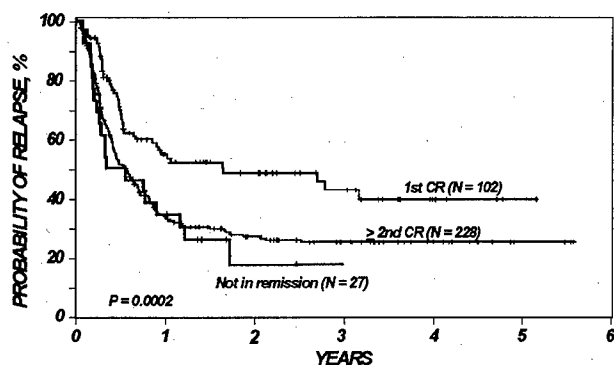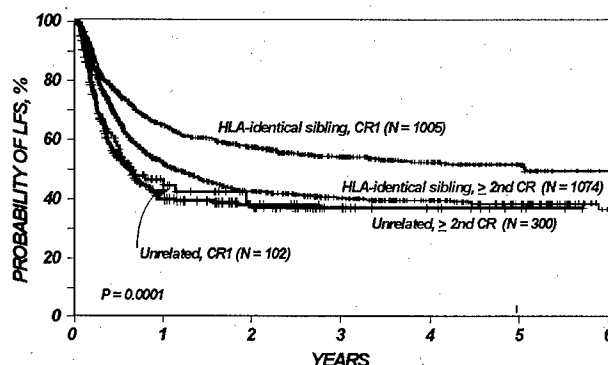
Slide 12. *Probability of Leukemia-free Survival after HLA-identical Sibling BMT for Acute Lymphoblastic Leukemia, 1989-1995*
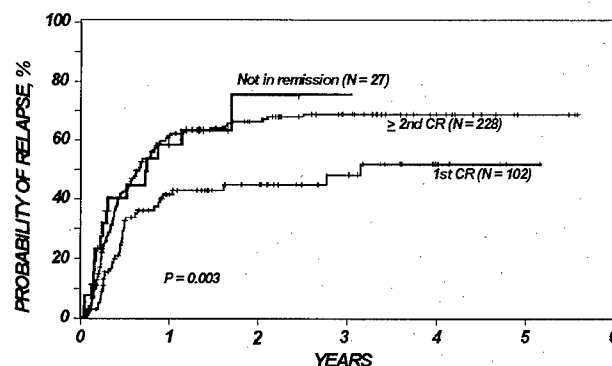
Slide 13. *Probability of Relapse after Autotransplants for Acute Lymphoblastic Leukemia, 1989-1995*

Slide 14. *Probability of Leukemia-free Survival after Autotransplants for Acute Lymphoblastic Leukemia, 1989-1995*

Slide 15. *Probability of Leukemia-free Survival after Allogeneic BMT for Acute Lymphoblastic Leukemia, 1989-1995*

Slide 15: Although associated with higher transplant-related mortality, unrelated donor transplants may be considered for patients with ALL unlikely to be cured with chemotherapy. Among 102 recipients of unrelated donor transplants for ALL in first remission reported to the IBMTR, 3-year LFS was 37 ± 14%; among 300 receiving unrelated donor transplants in second or subsequent remission, LFS was 36 ± 6%. Among patients transplanted in second remission, there was no difference in LFS between HLA-identical sibling and unrelated donor transplants, since higher GVHD rates were offset by lower relapse rates after unrelated donor transplants.

Slides 16, 17: As in ALL, results of HLA-identical sibling transplants for AML correlate with remission state. Among 3,503 recipients of HLA-identical sibling transplants done between 1989 and 1995, reported to the IBMTR, 3-year probabilities of relapse were 24 ± 2% for 2,247 transplants done in first remission, 45 ± 8% for 459 in second or subsequent remission and 57 ± 5% for 979 done in relapse. 3-year probabilities of LFS were 59 ± 2%, 35 ± 5% and 26 ± 4%, respectively.

Slides 18, 19: Among recipients of auto-transplants for AML between 1989 and 1995, reported to the ABMTR, 3-year probabilities

of relapse were 44 ± 4% for 858 transplants done in first remission, 56 ± 6% for 401 in second or subsequent remission and 83 ± 8% for 144 done in relapse. 3-year probabilities of LFS were 50 ± 4%, 38 ± 5% and 12 ± 7%, respectively.

Slide 20: As in ALL, unrelated donor transplants may be considered for some patients with AML lacking an HLA-identical sibling donor. Among 208 patients receiving unrelated donor transplants for AML between 1989 and 1995, reported to the IBMTR, the 3-year probability of LFS was 57 ± 13% for 87 receiving a transplant in first remission and 25 ± 12% for 121
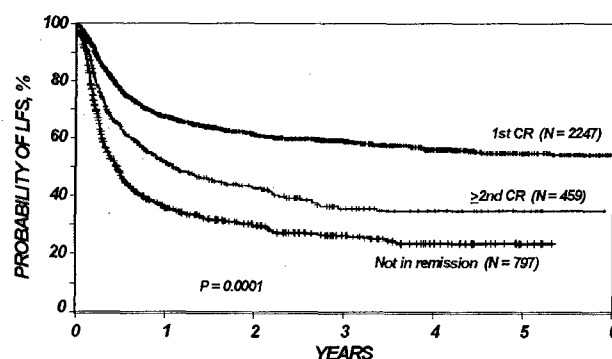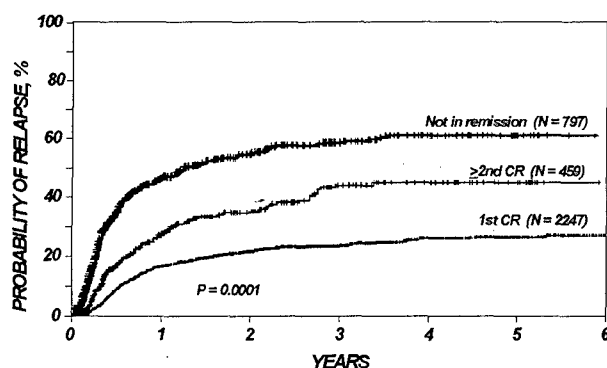
Slide 16. *Probability of Relapse after HLA-identical Sibling BMT for Acute Myelogenous Leukemia, 1989-1995*

Slide 17. *Probability of Leukemia-free Survival after HLA-identical Sibling BMT for Acute Myelogenous Leukemia, 1989-1995*
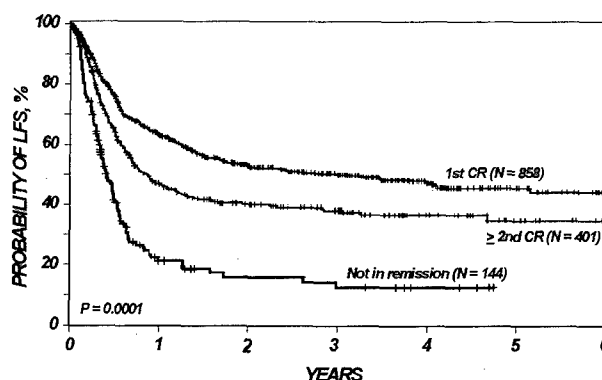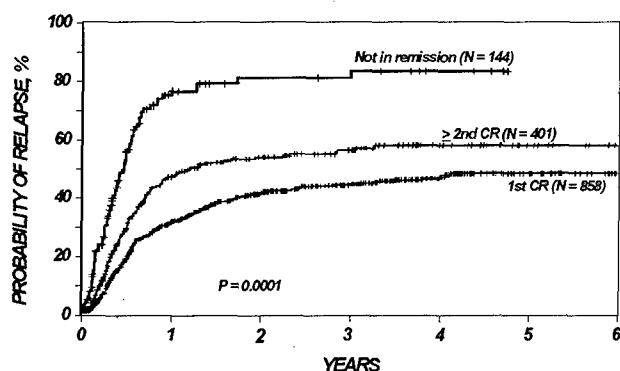
Slide 18. *Probability of Relapse after Autotransplants for Acute Myelogenous Leukemia, 1989-1995*

Slide 19. *Probability of Leukemia-free Survival after Autotransplants for Acute Myelogenous Leukemia, 1989-1995*

receiving a transplant in second or subsequent remission.

Slide 21: Bone marrow transplantation is the treatment of choice for young patients with aplastic anemia who have an HLA-identical sibling. 3-year probabilities of survival after 1,477 HLA-identical sibling transplants between 1989 and 1995, reported to the IBMTR, were 73 $\pm$ 4% for patients <20 years of age and 61 $\pm$ 5% for those older. Results were not as good in 200 recipients of unrelated donor transplants: 41 $\pm$ 10% in 136 patients <20 years and 40 $\pm$ 13% in 64 older patients.

Slide 22: Most patients with Hodgkin disease are cured with conventional chemotherapy. However, for the 20-30% failing conventional therapy, auto-transplants are effective salvage therapy. Among 993 autotransplants between 1989 and 1995, reported to the ABMTR, 3-year probabilities of survival were 86 $\pm$ 12% for 49 patients transplanted in first remission, 60 $\pm$ 6% for 463 transplanted in first relapse and 76 $\pm$ 8% for 224 transplanted in second or subsequent remission and 49 $\pm$ 9% for 257 patients never in remission.

Slide 23, 24: Autotransplants are also commonly used for non-Hodgkin lymphoma.

Among 407 patients receiving auto-transplants for low-grade lymphoma, 3-year probabilities of survival were 83 $\pm$ 14% for 64 patients transplanted in first remission, 67 $\pm$ 11% for 159 in first relapse, 65 $\pm$ 16% for 64 in second remission and 52 $\pm$ 16% for 120 never achieving remission with standard chemotherapy. Among 1,413 patients receiving autotransplants for intermediate grade or immunoblastic lymphoma, 3-year probabilities of survival were 68 $\pm$ 10% for 143 patients in first remission, 45 $\pm$ 5% for 594 in first relapse, 60 $\pm$ 8% for 250 in second remission and 40 $\pm$ 7% for 426 never
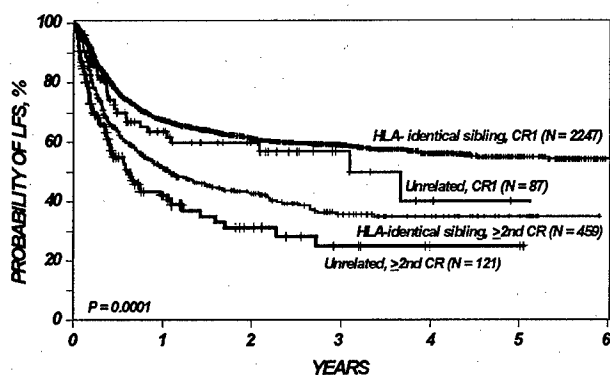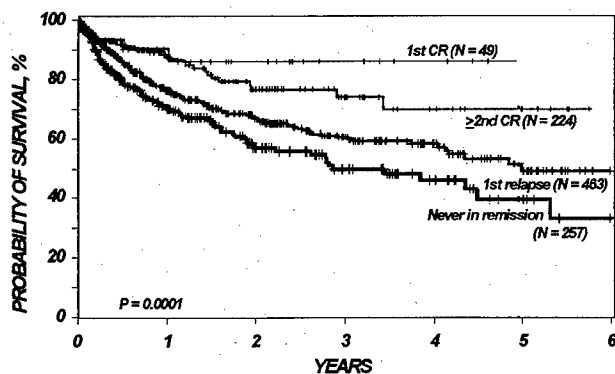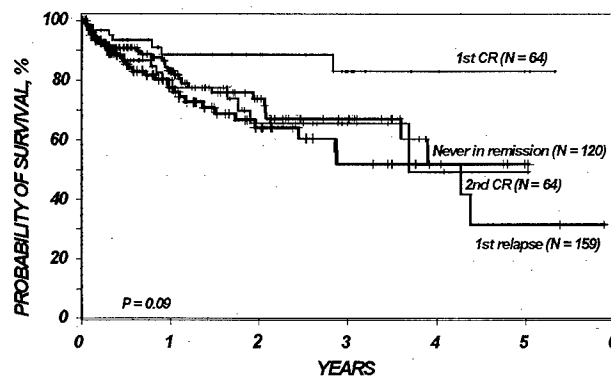
Slide 20. *Probability of Leukemia-free Survival after Allogeneic BMT for Acute Myelogenous Leukemia, 1989-1995*
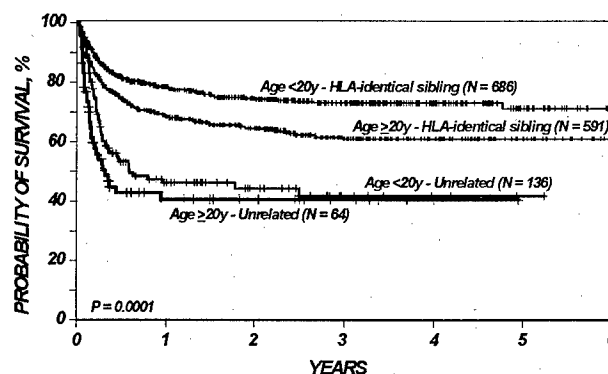
Slide 21. *Probability of Survival after HLA-identical Sibling and Unrelated BMT for Severe Aplastic Anemia, 1989-1995*

Slide 22. *Probability of Survival after Autotransplants for Hodgkin Disease, 1989-1995*

Slide 23. *Probability of Survival after Autotransplants for Low-Grade Non-Hodgkin Lymphoma, 1989-1995*

achieving remission with conventional chemotherapy. Most failures after autotransplants for non-Hodgkin lymphoma are due to relapse.

Slide 25, 26: Breast cancer is the most frequent indication for autotransplants in North America. Among 5,705 women receiving autotransplants for breast cancer between 1989 and 1995 and reported to the ABMTR, 3-year probabilities of survival were 74 ± 6% in 888 women with Stage 2 disease, 70 ± 7% in 749 women with Stage 3 disease, 51 ± 11% in 314 women with inflammatory breast cancer and 31 ± 2% in 3,754 women with metastatic breast cancer.

Outcome in metastatic breast cancer is significantly better for women achieving a complete response with conventional therapy prior to transplant. Among the 3,220 women transplanted for metastatic disease in whom pretransplant response to chemotherapy was known, 3-year survival was 45 ± 5% in 901 with a complete response, 27 ± 4% in 1,557 with a partial response and 17 ± 4% in 762 women with resistant disease.

Two sets of slides will be sent to participating teams of the IBMTR/ABMTR free of charge. Teams may purchase additional sets for $50.00.

If your budget does not permit this purchase, limited educational grants are available through the Statistical Center.

If you have any questions about our new slides, please call Melodee L. Nugent, MA at ☎(414) 456-8325.
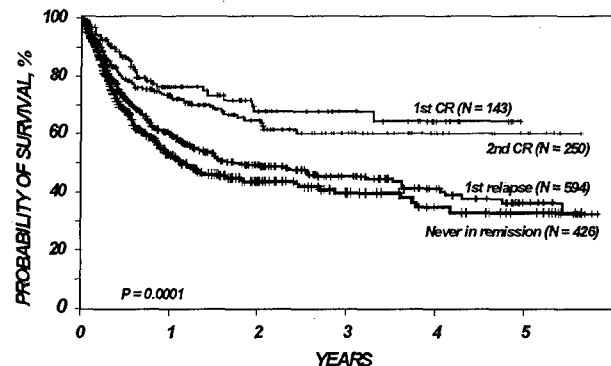
Slide 24. *Probability of Survival after Autotransplants for Intermediate Grade or Immunoblastic Non-Hodgkin Lymphoma, 1989-1995*
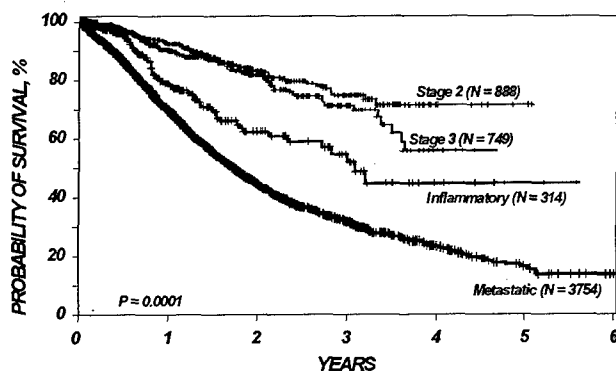
Slide 25. *Probability of Survival after Autotransplants for Breast Cancer, 1989-1995*
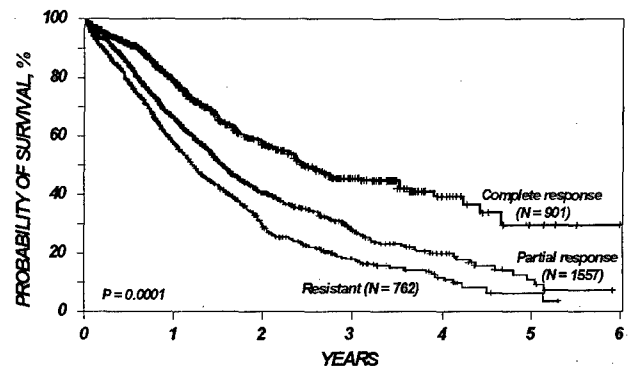
Slide 26. *Probability of Survival after Autotransplants for Metastatic Breast Cancer by Pretransplant Chemosensitivity, 1989-1995*

STATISTICAL METHODS
FOR ANALYZING TRANSPLANT OUTCOME

**By
John P. Klein, PhD**
*Statistical Director
IBMTR/ABMTR
Professor and Head,
Division of
Biostatistics at the
Medical College of
Wisconsin*

Transplant outcome depends on complex interactions among patient characteristics, disease biology and treatment. A statistical tool frequently used by the Statistical Center to study those interactions is regression analysis. Regression analyses examine the relationship between a set of factors (independent or explanatory variables) and an outcome (dependent or response variable). Explanatory variables may be patient and disease characteristics like age and disease stage and/or treatment strategies like conditioning regimen and growth factor use.

There are many techniques for regression analysis. The technique used for a specific study is determined by the outcome or response variable of interest. If the outcome is a continuous variable, e.g., days of hospitalization after high-dose therapy, <u>linear regression</u> is commonly used. Linear regression models consider the mean of the response variable as a linear function (sum) of a set of explanatory variables plus some measurement error. For example, a person's days in the hospital might be predicted by the sum of age, disease and growth factor use, each multiplied by an appropriate factor determined in the regression analysis.

For binary (yes/no) data (e.g., 100-day mortality), <u>logistic regression</u> is the most common approach. Logistic regression models the logarithm of the odds of an event occurring (yes response) as a linear function of the explanatory variables. The odds of an event occurring is the ratio of the probability of the event occurring divided by the probability of the event not occurring. When the independent variable is also binary, the logistic model also estimates the odds ratio for the independent variable. This gives a measure of how much more likely it is that an event will occur in an individual with a certain characteristic as compared to an individual without the characteristic. Logistic regression is available in many statistical packages. A good introductory book on this technique is Kleinbaum's *Logistic Regression: A Self Learning Text*, Springers Series on Statistics in the Health Sciences, 1994. Logistic regression techniques are also used to analyze matched-pairs data and analyze data where the response has more than two characteristics.

Most transplant studies focus on outcomes that involve time, e.g., time to engraftment, time to graft-versus-host disease (GVHD), time to disease recurrence, and time to death. The outcome measure has two aspects: whether or not the event occurs and the time at which it occurs. An important issue in these studies is that patients analyzed may be followed for different lengths of time (either because of entering the study at different times or loss to follow-up) or may die from another cause before the event occurs. These patients are *censored*. Whether they would have developed the event of interest with longer follow-up is unknown. For these situations, the technique most commonly used is *Cox* or *proportional hazards* regression.

Cox regression models the hazard rate of the time to occurrence of an event (hazard rate is the chance the event occurs at a given time for patients who have yet to experience the event). It assumes that for an individual with a given set of characteristics (explanatory variables), the hazard rate <u>at any point</u> in time can be obtained by multiplying a baseline hazard rate by the exponential of a linear function of the independent variables. It is called a proportional hazards model since individuals with distinct values of the independent covariates have hazard rates that are proportional at all points in time. The ratio of the hazard rates for such individuals is called the relative risk and gives a measure of how much more quickly individuals with one set of risk factors experience the event than individuals with some other set of risk factors. Cox regression is available in some of the standard statistical packages such as SAS and BMDP. It allows for the handling of censored data (data where some individuals do not experience the event) in a natural way. A good introductory reference on this techniques is the book by Kleinbaum on *Survival Analysis: A Self Learning Text*, Springers Series on Statistics in the Health Sciences, 1996.

Selection of the appropriate statistical model is crucial to avoid bias and maximize power to detect important relationships between explanatory and response variables. All models make some assumptions about these relationships (e.g., the assumption of proportionality for Cox models). Failure to check or meet these assumptions can produce misleading results. Though regression techniques are widely available in statistical packages, they should be used with guidance of persons with the statistical background to assure appropriate models are used correctly.

IBMTR/ABMTR Biostatisticians (left-right): Kathleen A. Sobocinski, MS; John P. Klein, PhD; Mei-Jie Zhang, PhD

RECENT SCIENTIFIC REPORTS FROM THE IBMTR/ABMTR

Gale RP, Horowitz MM, Rees JKH, Gray RG, Oken MM, Estey EH, Kim KM, Zhang MJ, Ash RC, Atkinson K, Champlin RE, Dicke KA, Gajewski JL, Goldman JM, Helbig W, Henslee-Downey PJ, Hinterberger W, Jacobsen N, Keating A, Klein JP, Marmont AM, Prentice HG, Reiffers J, Rimm AA, Rowlings PA, Sobocinski KA, Speck B, Wingard JR, Bortin MM. **Chemotherapy versus transplants for acute myelogenous leukemia in second remission.** Leukemia, 10:13-19, 1996.

Rozman C, Carreras E, Qian C, Gale RP, Bortin MM, Rowlings PA, Ash RC, Champlin RE, Henslee-Downey PJ, Herzig RH, Hinterberger W, Klein JP, Prentice HG, Reiffers J, Zwaan FE, Horowitz MM. **Risk factors for hepatic veno-occlusive disease following HLA-identical sibling bone marrow transplants for leukemia.** Bone Marrow Transplant, 17:75-80, 1996.

Gajewski JL, Phillips GL, Sobocinski KA, Armitage JO, Gale RP, Champlin RE, Herzig RH, Hurd DD, Jagannath S, Klein JP, Lazarus HM, McCarthy PL Jr., Pavlovsky S, Petersen FB, Rowlings PA, Russell JA, Silver SM, Vose JM, Wiernik PH, Bortin MM, Horowitz MM. **Bone marrow transplants from HLA-identical siblings in advanced Hodgkin's disease.** J Clin Oncol 14:572-578, 1996.

Michallet M, Archimbaud E, Bandini G, Rowlings PA, Deeg HJ, Gahrton G, Montserrat E, Rozman C, Gratwohl A, Gale RP, for the European Group for Blood and Marrow Transplantation and the International Bone Marrow Transplant Registry. **HLA-identical sibling bone marrow transplantation in younger patients with chronic lymphocytic leukemia.** Ann Intern Med 124:311-315, 1996.

Gale RP, Büchner T, Zhang MJ, Heinecke A, Champlin RE, Dicke KA, Gluckman E, Good RA, Gratwohl A, Herzig RH, Keating A, Klein JP, Marmont AM, Prentice HG, Rowlings PA, Sobocinski KA, Speck B, Weiner RS, Horowitz MM. **HLA-identical sibling bone marrow transplants versus chemotherapy for acute myelogenous leukemia in first remission.** Leukemia, 1996. *In press.*

Antman KH, Rowlings PA, Vaughan WP, Fay JW, Fields KK, Freytes CO, Gale RP, Hillner BE, Holland HK, Kennedy MJ, Klein JP, Lazarus HM, McCarthy PL, Pelz CJ, Saez R, Spitzer G, Stadtmauer EA, Williams SF, Wolff S, Sobocinski KA, Armitage JO, Horowitz MM. **High-dose chemotherapy with autologous hematopoietic stem cell support for breast cancer in North America.** J Clin Oncol, 1996. *In press.*

Hinterberger W, Rowlings PA, Hinterberger-Fischer M, Gibson J, Jacobsen N, Klein JP, Kolb HJ, Stevens DA, Horowitz MM, Gale RP. **Results of bone marrow transplants from genetically-identical twins in persons with aplastic anemia.** Ann Intern Med, 1996. *In press.*

Szydlo R, Goldman JM, Klein JP, Gale RP, Ash RC, Bach FH, Bradley BA, Casper JT, Flomenberg N, Gajewski JL, Gluckman E, Henslee-Downey PJ, Hows JM, Jacobsen N, Kolb H-J, Lowenberg B, Masaoka T, Rowlings PA, Sondel PM, van Bekkum DW, van Rood JJ, Vowels MR, Zhang MJ, Horowitz MM. **Results of allogeneic bone marrow transplants for leukemia using donors other than HLA-identical siblings.** J Clin Oncol, 1996. *In press.*

Passweg JR, Socié G, Hinterberger W, Bacigalupo A, Biggs JC, Camitta BM, Champlin RE, Gale RP, Gluckman E, Gordon-Smith EC, Hows JM, Klein JP, Nugent ML, Rowlings PA, Speck B, Tichelli A, Zhang MJ, Horowitz MM, Bortin MM. **Bone marrow transplantation for severe aplastic anemia: Has outcome improved?** Blood, 1996. *In press.*

Rowlings PA, Przepiorka D, Klein JP, Gale RP, Henslee-Downey PJ, Cahn JY, Calderwood S, Gratwohl A, Socié G, Abecasis MM, Passweg JR, Sobocinski KA, Zhang MJ, Horowitz MM. **A severity index for acute graft-versus-host disease.** Brit J Haematol, 1996. *In press.*

Horowitz MM, Rowlings PA, Passweg JR. **Allogeneic bone marrow transplantation for CML: a report from the International Bone Marrow Transplant Registry.** Bone Marrow Transplant 17 (Suppl 3): S5-S6, 1996.

Rowlings PA, Passweg JR, Armitage JO, Gale RP, Sobocinski KA, Klein JP, Zhang MJ, Horowitz MM. **Current status of allogeneic and autologous blood and marrow transplantation: Report from the IBMTR and ABMTR - North America.** In: Yearbook of Cell and Tissue Transplantation (Lanza RP, Chick WL, eds), Kluwer Academic Publishers, the Netherlands, 1996, pp 19-34.

REPRINTS AVAILABLE ON REQUEST

Annual Meeting... (continued from page 1)

- Assistance with flights to Sky Harbor International Airport in Phoenix is available through Meetings & Incentives ☎ (414) 835-3553 ext.126 or (800) 776-3582 ext.126.

- Sky Harbor Airport is an easy 20 minute drive to the Radisson Resort Scottsdale. Special rental discounts available through Hertz—the official car rental company: ☎ (800) 654-2240; refer to CV#17584.

IBMTR/ABMTR Working Committee meetings are open to those interested in *actively* participating in ongoing and future Registry studies. All Working Committee members should plan to attend.

Fifty $500 grants were recently awarded to persons registered for the Data Management Workshops on Saturday, February 22. Grant funds were provided by the US Department of the Army for teams submitting breast cancer data to the ABMTR. The Data Management Workshops are designed specifically for clinical research associates, data managers, nurses and others interested in data management. Fundamentals of Registry data management and special topics related to clinical research will be covered.

StemCell Technologies, Inc. will offer "hands-on" training for StemSoft data entry software on Sunday, February 23. Call Violet Molnar in Vancouver, BC at ☎ (604) 877-0713 to register. The fee for this additional session is US $300.

All members of IBMTR and ABMTR-North America participating bone marrow transplant teams are encouraged to attend. We hope to have each team represented at the 1997 Meeting.

Detailed meeting brochures available, please contact: D'Etta Waldoch Koser, CMP, at the Statistical Center; ☎ **(414) 456-8377,** fax: **(414) 266-8471,** or email: **ibmtrdwk@hp04.biostat.mcw.edu**

FOUNDATION AND CORPORATE SUPPORT OF THE IBMTR/ABMTR

By Susan Ladwig, MA Associate Director of Development, Statistical Center

All of us at the IBMTR/ABMTR Statistical Center thank the many contributors who have joined our international collaboration for research in blood and marrow transplantation. Private support for the Registries continues to be vitally important since federal grants cover only 60 percent of the Statistical Center's budget. We gratefully acknowledge the support of the Medical College of Wisconsin; the National Cancer Institute; the National Institute of Allergy and Infectious Disease; the National Heart, Lung and Blood Institute; the Department of Defense; and the generosity of the following foundations and corporations:

NON-FEDERAL SUPPORT LISTING FOR THE IBMTR/ABMTR (GRANT AWARDS SINCE 1993)

Activated Cell Therapy, Inc.
* Alpha Therapeutic Corporation
Alpha Therapeutic GmbH
* American Oncology Resources
* Amgen, Inc.
Amgen Europe AG
Astra Arcus AB
* Astra USA
Baxter Healthcare Corporation
* Bayer Corporation
Biogen
BIS Laboratories
* Blue Cross and Blue Shield Association
The Lynde and Harry Bradley Foundation
* Bristol-Myers Squibb Company
Caremark, Inc.
Cell Therapeutics, Inc.
* CellPro, Inc.
* Centeon
Center for Advanced Studies in Leukemia
* Chiron Therapeutics
Cigna Health Care
* COBE BCT Inc.
* Coram Healthcare
Charles E. Culpeper Foundation
Eleanor Naylor Dana Charitable Trust

Deborah J. Dearholt Memorial Fund
The Eppley Foundation for Research
ESSEX Pharma GmbH (Germany)
Fujisawa USA
Genentech, Inc.
Glaxo Wellcome Company
Hewlett-Packard Company
Hoechst Marion Roussel, Inc.
* Immunex Corporation
* Janssen Pharmaceutica
The Kettering Family Foundation
Kirin Brewery Company (Japan)
Robert J. Kleberg, Jr. & Helen C. Kleberg Foundation
Herbert H. Kohl Charities
Lederle International
Life Technologies, Inc.
Eli Lilly Company Foundation
* The Liposome Company
Nada and Herbert P. Mahler Charities
Medical SafeTEC
* MGI Pharma, Inc.
* Milliman & Robertson, Inc.
Milstein Family Foundation
The Milwaukee Foundation/ Elsa Schoeneich Medical Research Fund
NCGS and Associates, Inc.
NeXstar Pharmaceuticals, Inc.

* Corporate Member

Samuel Roberts Noble Foundation
* Ortho Biotech
John Oster Family Foundation
Elsa U. Pardee Foundation
Jane & Lloyd Pettit Foundation
Alirio Pfiffer Bone Marrow Transplantation Support Association
* Pfizer Inc.
Pharmacia and Upjohn
QLT PhotoTherapeutics, Inc.
Quantum Health Resources
RGK Foundation
Roche Laboratories
* RPR Gencell
Sandoz Pharmaceuticals Corporation
* SangStat Medical Corporation
* Schering-Plough International
Walter Schroeder Foundation, Inc.
* Searle
SEQUUS Pharmaceuticals
Stackner Family Foundation
The Starr Foundation
Joan and Jack Stein Charities
StemCell Technologies, Inc.
SyStemix
Therakos
Laboratories Wyeth France
* Wyeth-Ayerst Laboratories
* Xoma Corporation

A special thank you to our 1997 Annual Meeting Sponsors

Amgen, Inc.
Baxter Healthcare, Inc., Biotech Group
BIS Laboratories
Bristol-Myers Oncology
Cell Therapeutics, Inc.
CellPro, Inc.
Centeon
Chiron Therapeutics
COBE BCT, Inc.
Fujisawa USA, Inc.
Immunex Corporation
Janssen Pharmaceutica
Life Technologies, Inc.
The Liposome Company, Inc.
Medical SafeTEC
NeXstar Pharmaceuticals, Inc.
NCGS and Associates, Inc.
Ortho Biotech
Pfizer, Inc.
Pharmacia & Upjohn, Inc.
QLT PhotoTherapeutics, Inc.
Quantum Health Resources
Roche Laboratories
Sandoz Oncology
Searle
SEQUUS Pharmaceuticals
StemCell Technologies
SyStemix
TS Scientific and Planer Products
Wyeth-Ayerst Laboratories

STATISTICAL CENTER INITIATES CORPORATE MEMBERSHIP PROGRAM

Several corporations have joined the newly established IBMTR/ABMTR Corporate Membership Program (see above listing). The annual membership program provides member organizations with informational materials on blood and bone marrow transplantation developed by the IBMTR/ABMTR Information Resource Service.

The program includes subscriptions to the *Statistical Center Report on Survival Statistics for Blood and Marrow Transplants, IBMTR and ABMTR Newsletters,* the worldwide *IBMTR/ABMTR Directory of Bone Marrow Transplant Teams,* and the *IBMTR/ABMTR Summary Slides on State-of-the-Art in Blood and Marrow Transplantation* as well as invitations to our meetings and educational forums and access to the IBMTR/ABMTR databases for simple analyses. These resources are useful for marketing managers, medical directors, research directors, product managers, case managers or transplant coordinators.
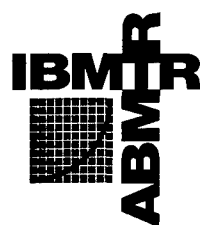
For additional information on the Corporate Membership Program, please contact Susan Ladwig, Associate Director of Development ☎ (414) 456-8363, Fax: (414) 266-8471.

STATISTICAL CENTER PERSONNEL

MARY M. HOROWITZ, MD, MS
Scientific Director

PHILIP A. ROWLINGS, MD, MS
Assistant Scientific Director

MARLIES E.H.M. VAN HOEF, MD
Visiting Assistant Professor

JOHN P. KLEIN, PhD
Statistical Director

MEI-JIE ZHANG, PhD
Assistant Professor/Biostatistician

KATHLEEN A. SOBOCINSKI, MS
Associate Statistical Director

MELODEE L. NUGENT, MA
Information Specialist/Biostatistician

SANDRA C. MURPHY, MS
Biostatistician

JUDY VEUM STONE, MS
Biostatistician

COREY J. PELZ, MS
Biostatistician

BARBARA A. MCGARY, BS
Manager of Information Systems

BARBARA B. LIU, MS
Database Programs Manager

SHARON K. NELL
Communications Coordinator

JANE E. REBRO
Assistant Communications Coordinator

DIANE J. KNUTSON
Systems Coordinator

CLAUDIA A. ABEL
Data Coordinator

ANGELA S. KUMMEROW
Data Coordinator

HONGYU TIAN
Data Coordinator

PATRICIA A. VESPALEC
Data Coordinator

BARBARA BORTIN, MS
Data Entry Assistant

WENDY CHAI
Data Entry Assistant

YING HU
Data Entry Assistant

LILY QIAN
Data Entry Assistant

ANN G. PERELES
Data Entry Assistant

JANELLE M. STANO
Data Entry Assistant

D'ETTA WALDOCH KOSER, CMP
Associate Director,
International Programs

LAURIE L. SCHWEITZER
Clerical Assistant

SUSAN U. LADWIG, MA
Associate Director of Development

LISA J. LEHRMANN
Program Coordinator

LINDA M. SCHNEIDER
Desktop Publishing Specialist

KIM R. HYLER
Administrative Assistant

JEAN M. EDER
Staff Assistant

ABMTR ADVISORY COMMITTEE

James O. Armitage, MD
(Chair)
University of Nebraska
Medical Center
Omaha, NE, USA

Karen Antman, MD
Columbia University
New York, NY, USA

Frederick R. Appelbaum, MD
Fred Hutchinson
Cancer Research Center
Seattle, WA, USA

Charles S. August, MD
Miami Children's Hospital
Miami, FL, USA

Karl G. Blume, MD
Stanford University
Medical Center
Stanford, CA, USA

Bruce Camitta, MD
Medical College of Wisconsin
Milwaukee, WI, USA

Richard E. Champlin, MD
MD Anderson Cancer Center
Houston, TX, USA

Paul A. Chervenick, MD
H. Lee Moffitt
Cancer Center
Tampa, FL, USA

Peter F. Coccia, MD
University of Nebraska
Medical Center
Omaha, NE, USA

Karel A. Dicke, MD, PhD
Arlington Cancer Center
Arlington, TX, USA

Gerald J. Elfenbein, MD
H. Lee Moffitt
Cancer Center
Tampa, FL, USA

Joseph W. Fay, MD
Baylor University
Medical Center
Dallas, TX, USA

Robert Peter Gale, MD, PhD
Salick Health Care, Inc.
Los Angeles, CA, USA

John Graham-Pole, MD
University of Florida
Gainesville, FL, USA

Subhash C. Gulati, MD
New York Hospital/Cornell
Medical Center
New York, NY, USA

Geoffrey P. Herzig, MD
Roswell Park Cancer Institute
Buffalo, NY, USA

Roger H. Herzig, MD
Jewish Hospital of Cincinnati
Cincinnati, OH, USA

Mary M. Horowitz, MD, MS
Medical College of Wisconsin
Milwaukee, WI, USA

David D. Hurd, MD
Wake Forest University
Cancer Center
Winston-Salem, NC, USA

Sundar Jagannath, MD
University of Arkansas
Medical School
Little Rock, AK, USA

Herbert Kaizer, MD
Rush Presbyterian
St. Luke's Medical Center
Chicago, IL, USA

Armand Keating, MD
University of Toronto
Toronto, Ontario, Canada

John P. Klein, PhD
Medical College of Wisconsin
Milwaukee, WI, USA

Hillard M. Lazarus, MD
University Hospital
of Cleveland
Cleveland, OH, USA

Carole B. Miller, MD
Johns Hopkins
Oncology Center
Baltimore, MD, USA

Lee M. Nadler, MD
Dana-Farber Cancer Institute
Boston, MA, USA

Gordon L. Phillips, MD
Markey Cancer Center
Lexington, KY, USA

Norma K. C. Ramsay, MD
University of Minnesota
Minneapolis, MN, USA

Robert C. Seeger, MD
Children's Hospital
of Los Angeles
Los Angeles, CA, USA

Elizabeth J. Shpall, MD
University of Colorado
Health Sciences Center
Denver, CO, USA

Gary L. Spitzer, MD
Intermountain Health Care
Sale Lake City, UT, USA

Patrick J. Stiff, MD
Loyola University
Maywood, IL, USA

William P. Vaughan, MD
University of Alabama
at Birmingham
Birmingham, AL, USA

Julie M. Vose, MD
University of Nebraska
Medical Center
Omaha, NE, USA

Roy S. Weiner, MD
Tulane University
School of Medicine
New Orleans, LA, USA

Daniel J. Weisdorf, MD
University of Minnesota
Minneapolis, MN, USA

Stephanie F. Williams, MD
Univeristy of Chicago
Medical Center
Chicago, IL, USA

Steven N. Wolff, MD
Vanderbilt University
Medical Center
Nashville, TN, USA
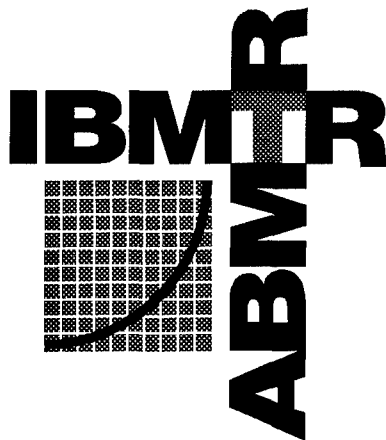
IBMTR
International Bone Marrow Transplant Registry

ABMTR
Autologous Blood and Marrow Transplant Registry

1996 IBMTR / ABMTR Summary Slides

Current Status of

Blood & Marrow Transplantation

Supported by an educational grant from
Bristol-Myers Squibb Company

PLEASE NOTE: THE ENCLOSED
ABMTR NEWSLETTER INCLUDES A
GUIDE TO THE SUMMARY SLIDES

ANNUAL NUMBER OF
BLOOD AND MARROW TRANSPLANTS
WORLDWIDE
1970-1995

Sum23.ppt

STEM CELL SOURCES
1995

% OF TRANSPLANTS

BONE MARROW
BLOOD
BONE MARROW & BLOOD
UMBILICAL CORD BLOOD

AUTOLOGOUS   ALLOGENEIC

Sum35.ppt

PERCENT OF ALLOGENEIC TRANSPLANTS FROM UNRELATED DONORS

% OF TRANSPLANTS

100 · 80 · 60 · 40 · 20 · 0

3269 — 1985-86
3884 — 1987-88
5921 — 1989-90
7148 — 1991-92
8313 — 1993-94
5210* — 1995-96

Numbers on bars = numbers of patients evaluable

* 1996 data incomplete

EDI_7.wmf

ABMTR
IBMTR

INDICATIONS FOR BLOOD AND MARROW TRANSPLANTATION IN NORTH AMERICA
1995

Sum24.ppt
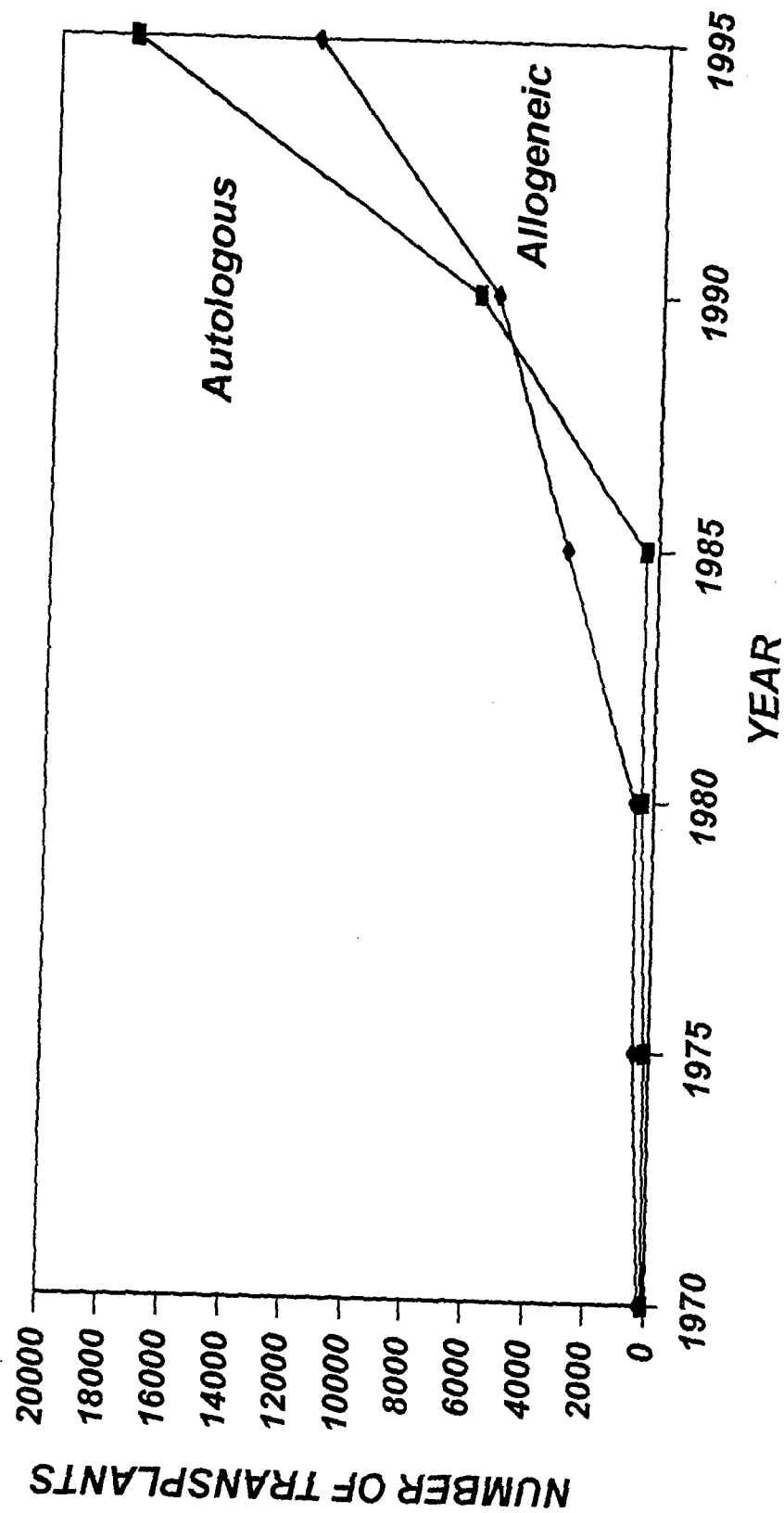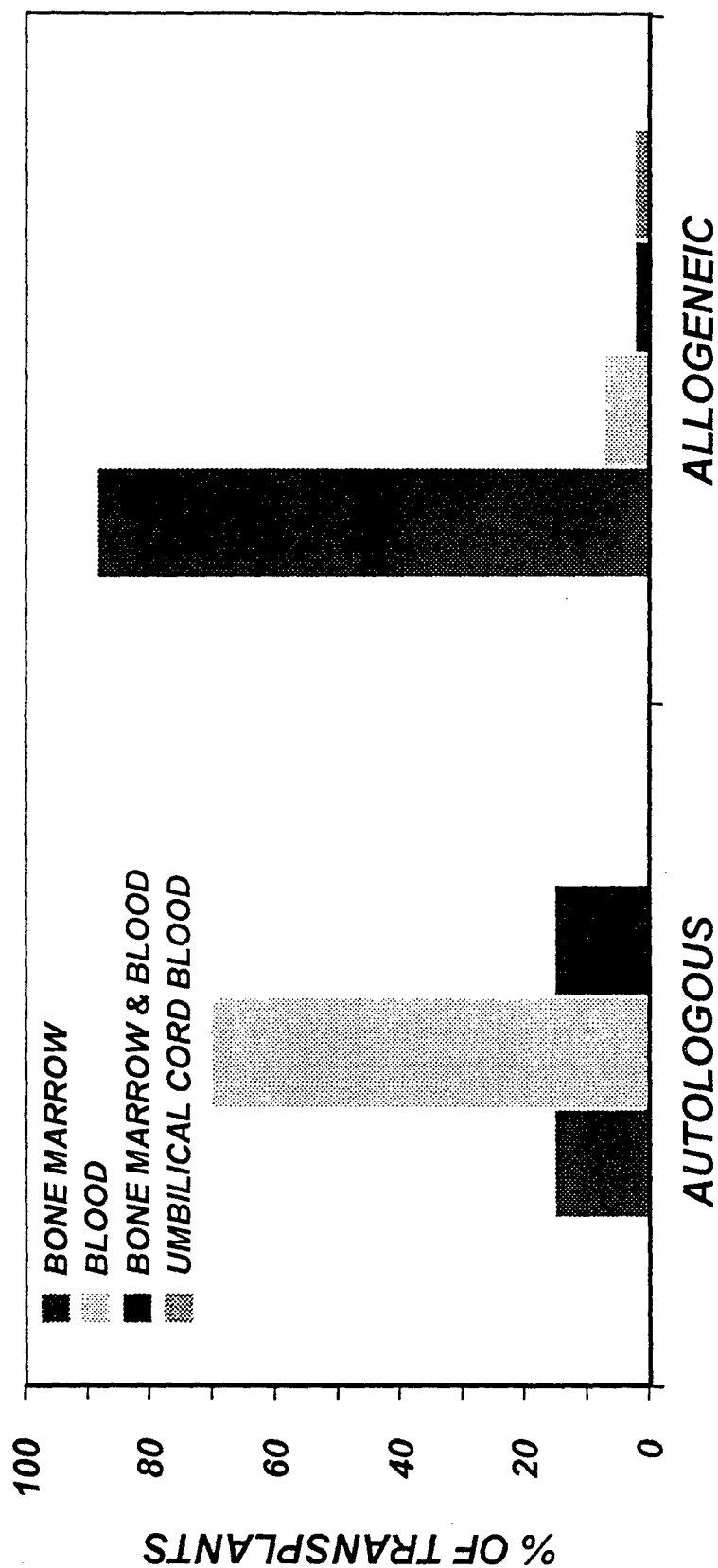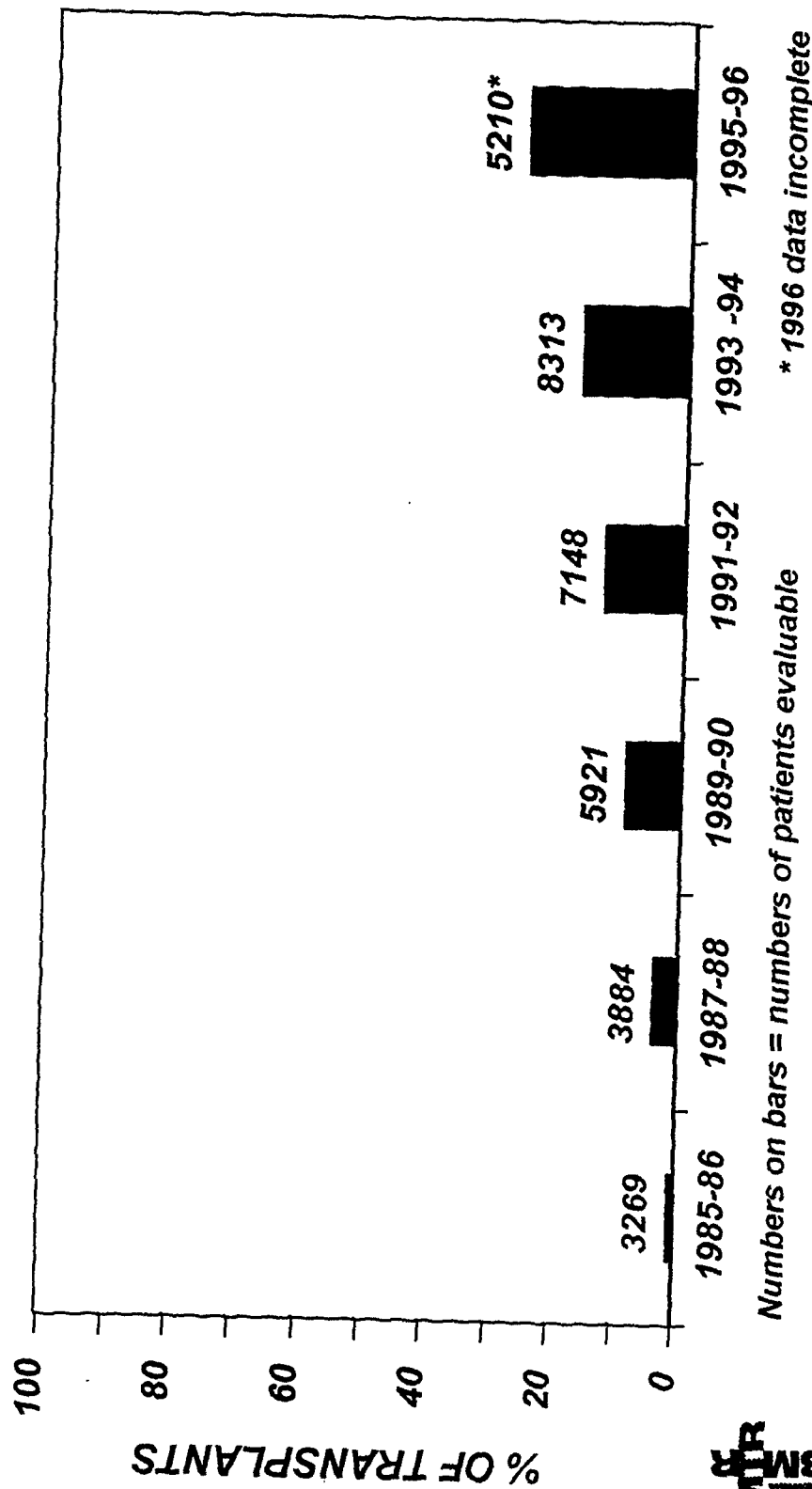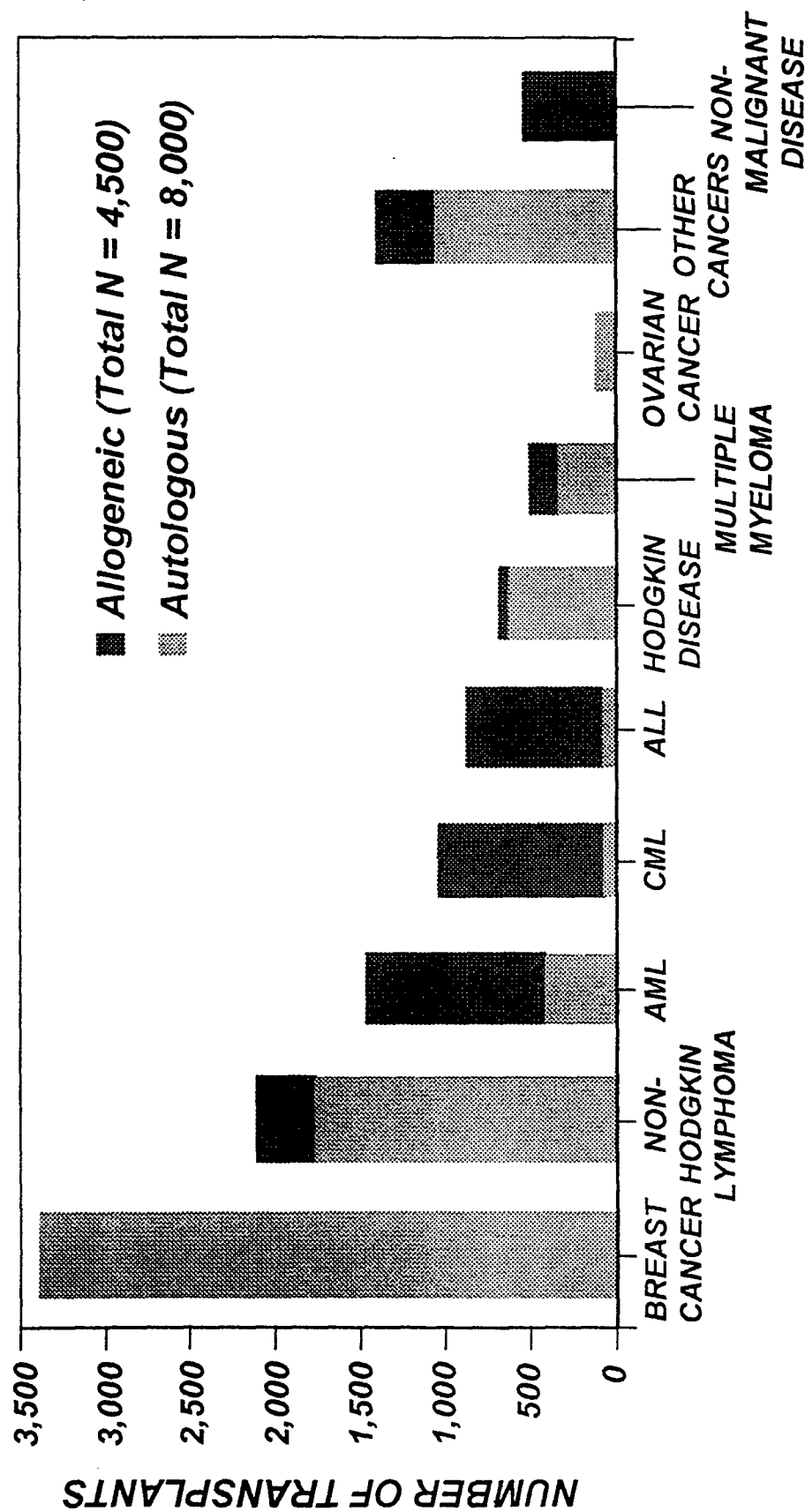
100-DAY MORTALITY AFTER HLA-IDENTICAL SIBLING TRANSPLANTS 1995

Numbers on bars = numbers of patients evaluable

Sum36.ppt

100-DAY MORTALITY
AFTER AUTOTRANSPLANTS
1995

Stage 2-3
Metastatic
Any CR
Not in CR

ACUTE LEUKEMIA   236   86

NON-HODGKIN LYMPHOMA   250   616

HODGKIN DISEASE   104   227

BREAST CANCER   694   1000

MORTALITY RATE, %

Numbers on bars = numbers of patients evaluable

IBMTR / ABMTR

SUM37.wmf

PROBABILITY OF RELAPSE AFTER
HLA-IDENTICAL SIBLING BMT FOR
CHRONIC MYELOGENOUS LEUKEMIA
1989-1995

P = 0.0001

Blast Phase (N = 166)

Accelerated Phase (N = 490)

Chronic Phase (N = 2753)

PROBABILITY OF
RELAPSE, %

YEARS

SUM15.wmf

PROBABILITY OF LEUKEMIA-FREE SURVIVAL
AFTER HLA-IDENTICAL SIBLING BMT FOR
CHRONIC MYELOGENOUS LEUKEMIA
1989-1995

Chronic Phase (N = 2753)

Accelerated Phase (N = 490)

Blast Phase (N = 166)

P = 0.0001

PROBABILITY OF LFS, %

YEARS

Sum16.ppt

PROBABILITY OF SURVIVAL AFTER
HLA-IDENTICAL SIBLING BMT FOR
CHRONIC MYELOGENOUS LEUKEMIA
1989-1995

Chronic Phase (N = 2753)

Accelerated Phase (N = 490)

Blast Phase (N = 166)

P = 0.0001

PROBABILITY OF
SURVIVAL, %

YEARS

Surv40.ppt
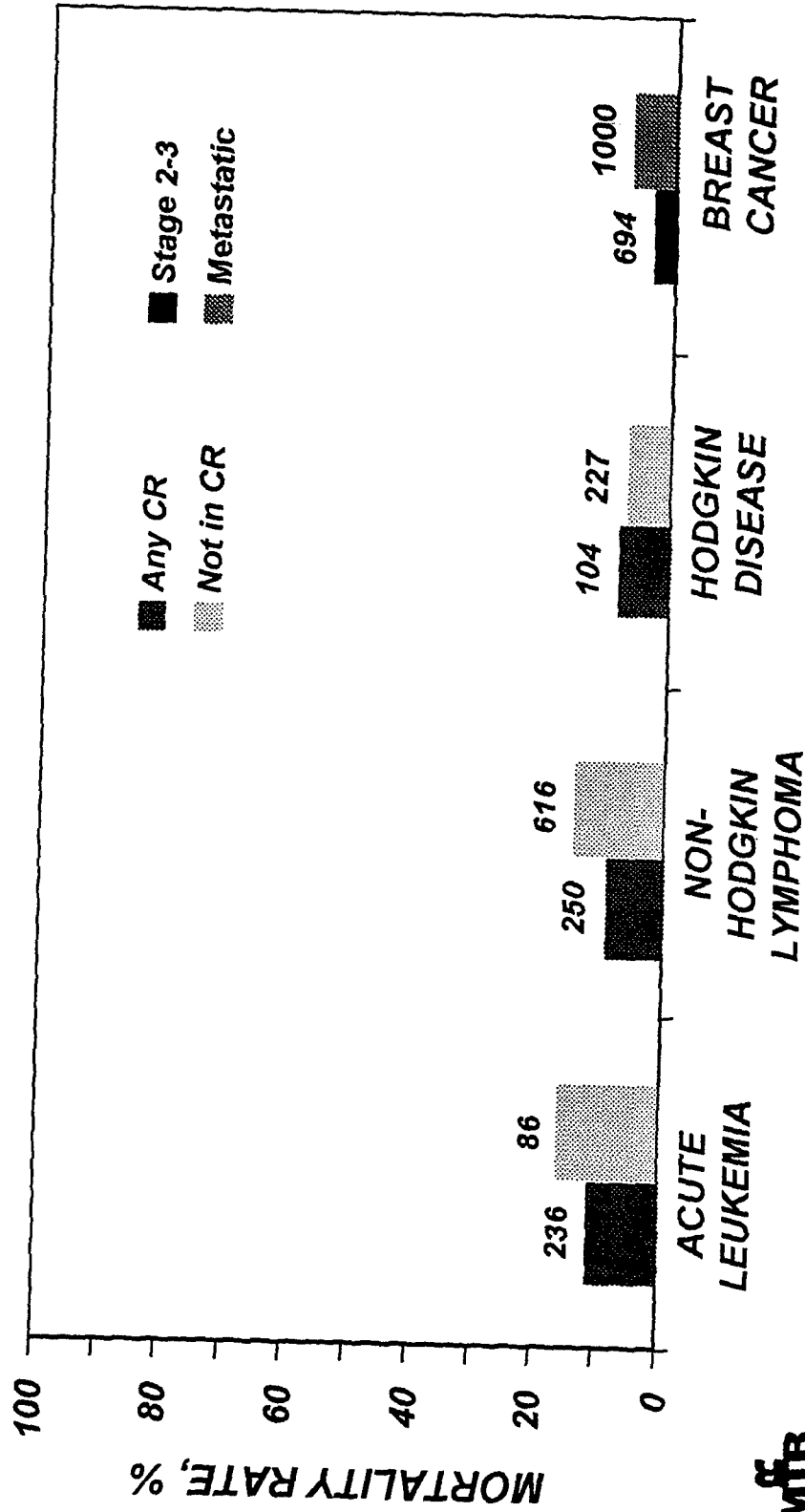
PROBABILITY OF LFS AFTER BMT FOR
CHRONIC MYELOGENOUS LEUKEMIA
IN CHRONIC PHASE
- Interval Diagnosis to Transplant -

PROBABILITY OF RELAPSE AFTER HLA-IDENTICAL SIBLING BMT FOR ACUTE LYMPHOBLASTIC LEUKEMIA 1989-1995

Not in remission (N = 418)

≥ 2nd CR (N = 1074)

1st CR (N = 1005)

P = 0.0001

PROBABILITY OF RELAPSE, %

YEARS

Sum_7.ppt

PROBABILITY OF LEUKEMIA-FREE SURVIVAL AFTER HLA-IDENTICAL SIBLING BMT FOR ACUTE LYMPHOBLASTIC LEUKEMIA 1989-1995

1st CR (N = 1005)

≥ 2nd CR (N = 1074)

Not in remission (N = 418)

P = 0.0001

PROBABILITY OF LFS, %

YEARS

Sum_8.ppt

PROBABILITY OF RELAPSE
AFTER AUTOTRANSPLANTS FOR
ACUTE LYMPHOBLASTIC LEUKEMIA
1989-1995

Not in remission (N = 27)

≥ 2nd CR (N = 228)

1st CR (N = 102)

P = 0.003

PROBABILITY
OF RELAPSE, %

YEARS

PROBABILITY OF LEUKEMIA-FREE SURVIVAL
AFTER AUTOTRANSPLANTS FOR
ACUTE LYMPHOBLASTIC LEUKEMIA
1989-1995

Sum10.ppt

PROBABILITY OF LEUKEMIA-FREE SURVIVAL
AFTER ALLOGENEIC BMT FOR
ACUTE LYMPHOBLASTIC LEUKEMIA
1989-1995

HLA-identical sibling, CR1 (N = 1005)

HLA-identical sibling, ≥ 2nd CR (N = 1074)

Unrelated, ≥ 2nd CR (N = 300)

Unrelated, CR1 (N = 102)

P = 0.0001

PROBABILITY OF LFS, %

100
80
60
40
20
0

0   1   2   3   4   5   6

YEARS

Sum39.ppt

PROBABILITY OF RELAPSE AFTER
HLA-IDENTICAL SIBLING BMT FOR
ACUTE MYELOGENOUS LEUKEMIA
1989-1995

Not in remission (N = 797)

>2nd CR (N = 459)

1st CR (N = 2247)

P = 0.0001

YEARS

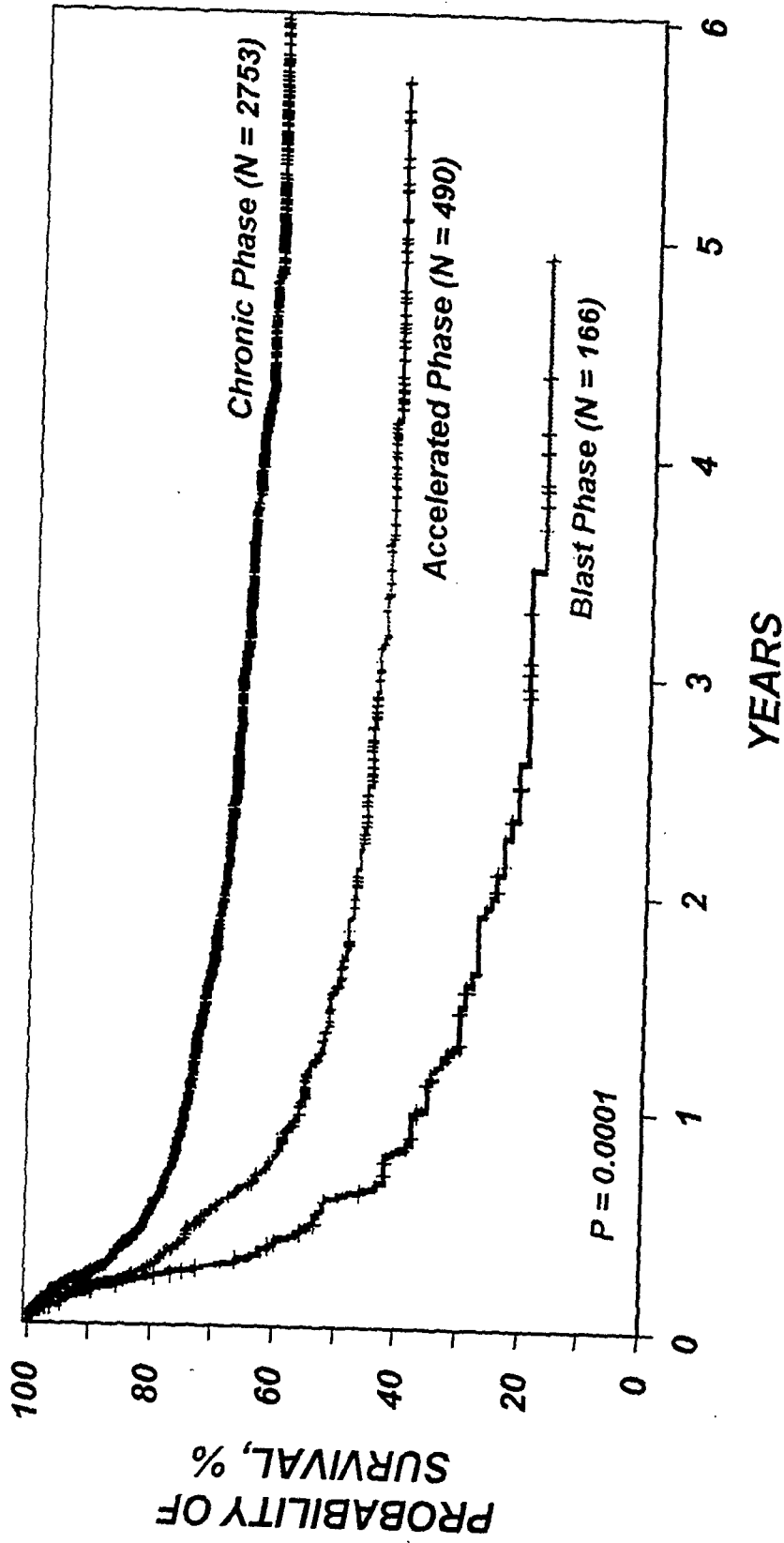PROBABILITY OF RELAPSE, %

Sumff.ppt

PROBABILITY OF LEUKEMIA-FREE SURVIVAL
AFTER HLA-IDENTICAL SIBLING BMT FOR
ACUTE MYELOGENOUS LEUKEMIA
1989-1995

Sum12.ppt

PROBABILITY OF RELAPSE
AFTER AUTOTRANSPLANTS FOR
ACUTE MYELOGENOUS LEUKEMIA,
1989-1995

Not in remission (N = 144)

≥ 2nd CR (N = 401)

1st CR (N = 858)

P = 0.0001

PROBABILITY OF RELAPSE, %

100   80   60   40   20   0

0   1   2   3   4   5   6

YEARS

Sum13.ppt

PROBABILITY OF LEUKEMIA-FREE SURVIVAL AFTER AUTOTRANSPLANTS FOR ACUTE MYELOGENOUS LEUKEMIA 1989-1995

1st CR (N = 858)

≥ 2nd CR (N = 401)

Not in remission (N = 144)

P = 0.0001

PROBABILITY OF LFS, %

YEARS

PROBABILITY OF LEUKEMIA-FREE SURVIVAL AFTER ALLOGENEIC BMT FOR ACUTE MYELOGENOUS LEUKEMIA 1989-1995

PROBABILITY OF SURVIVAL AFTER HLA-IDENTICAL SIBLING AND UNRELATED BMT FOR SEVERE APLASTIC ANEMIA 1989 - 1995

Age <20y, HLA-identical sibling (N = 686)

Age ≥20y, HLA-identical sibling (N = 591)

Age <20y, Unrelated (N = 136)

Age ≥20y, Unrelated (N = 64)

P = 0.0001

PROBABILITY OF SURVIVAL, %

YEARS

ABMTR

SUM43.wmf

PROBABILITY OF SURVIVAL AFTER
AUTOTRANSPLANTS FOR HODGKIN DISEASE
1989-1995

PROBABILITY OF SURVIVAL, %

YEARS

1st CR (N = 49)

≥2nd CR (N = 224)

1st relapse (N = 463)

Never in remission (N = 257)

P = 0.0001

Sum18.ppt
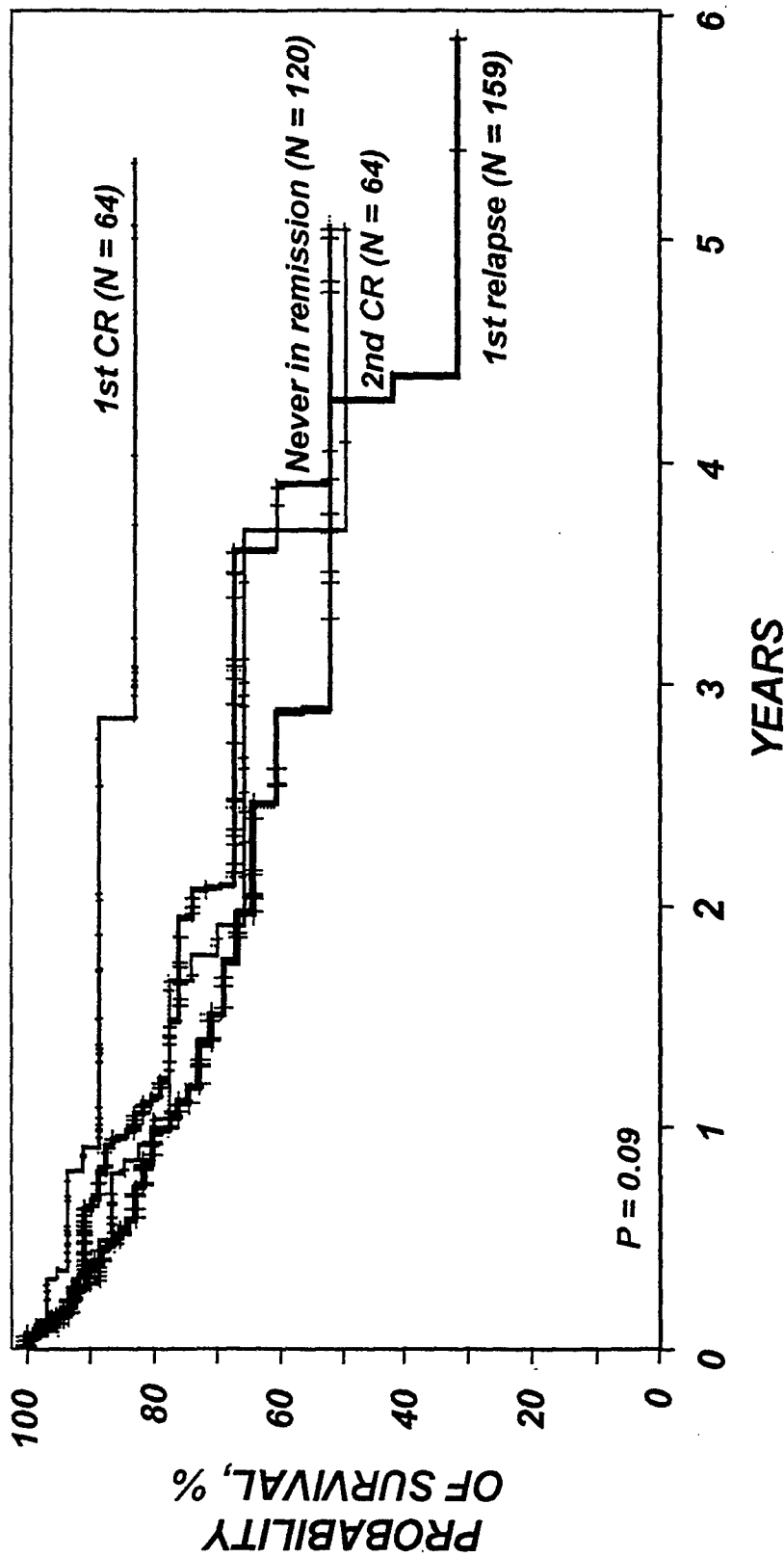
PROBABILITY OF SURVIVAL AFTER
AUTOTRANSPLANTS FOR LOW-GRADE
NON-HODGKIN LYMPHOMA
1989-1995

PROBABILITY OF SURVIVAL AFTER
AUTOTRANSPLANTS FOR INTERMEDIATE GRADE
OR IMMUNOBLASTIC NON-HODGKIN LYMPHOMA
1989-1995
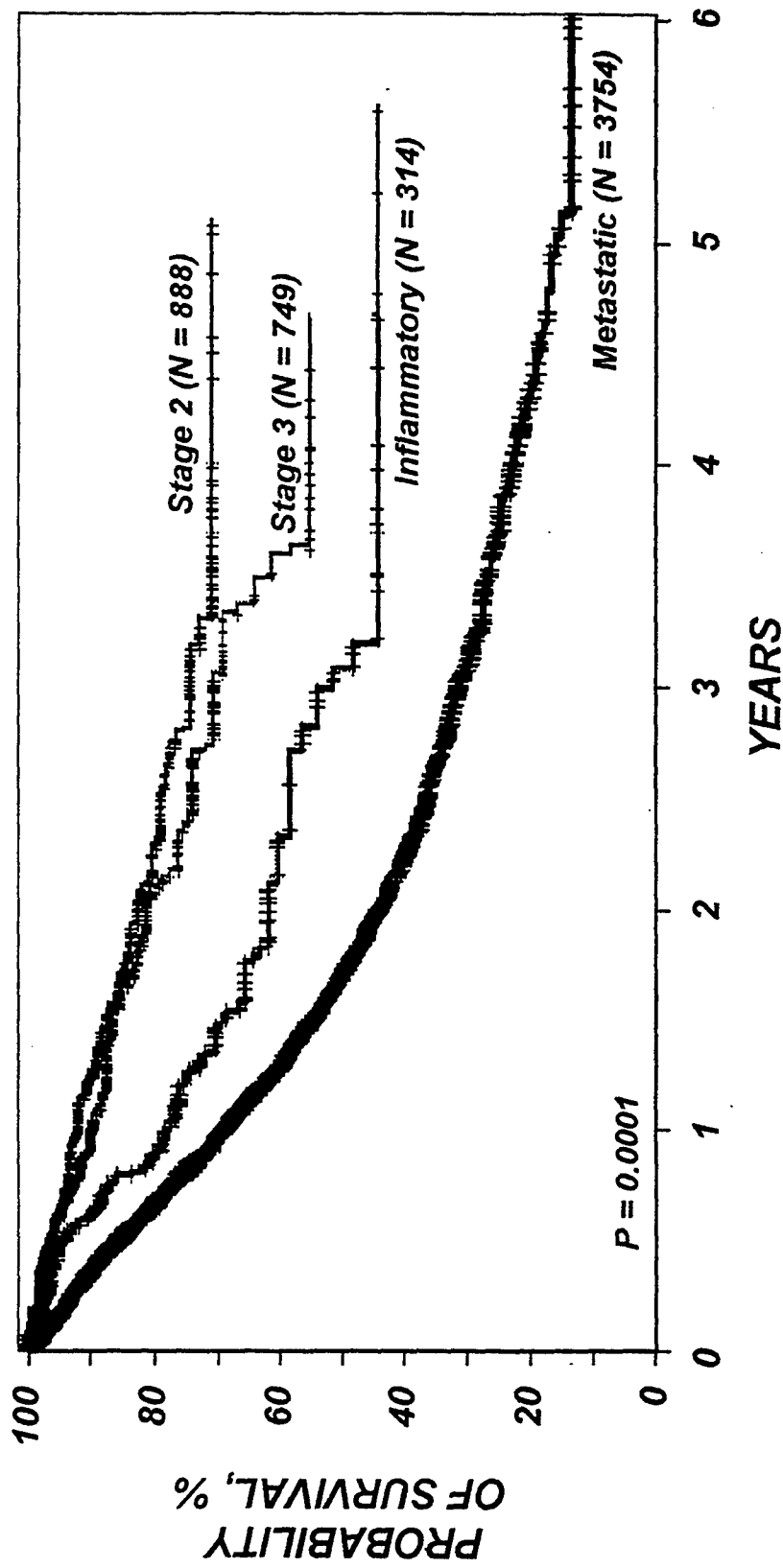
1st CR (N = 143)

2nd CR (N = 250)

1st relapse (N = 594)

Never in remission (N = 426)

P = 0.0001

PROBABILITY OF SURVIVAL, %

YEARS

Sum20.ppt

PROBABILITY OF SURVIVAL AFTER AUTOTRANSPLANTS FOR BREAST CANCER 1989-1995

PROBABILITY OF SURVIVAL AFTER
AUTOTRANSPLANTS FOR METASTATIC BREAST CANCER
- Pretransplant Response to Chemotherapy -
1989-1995

Appendix 7
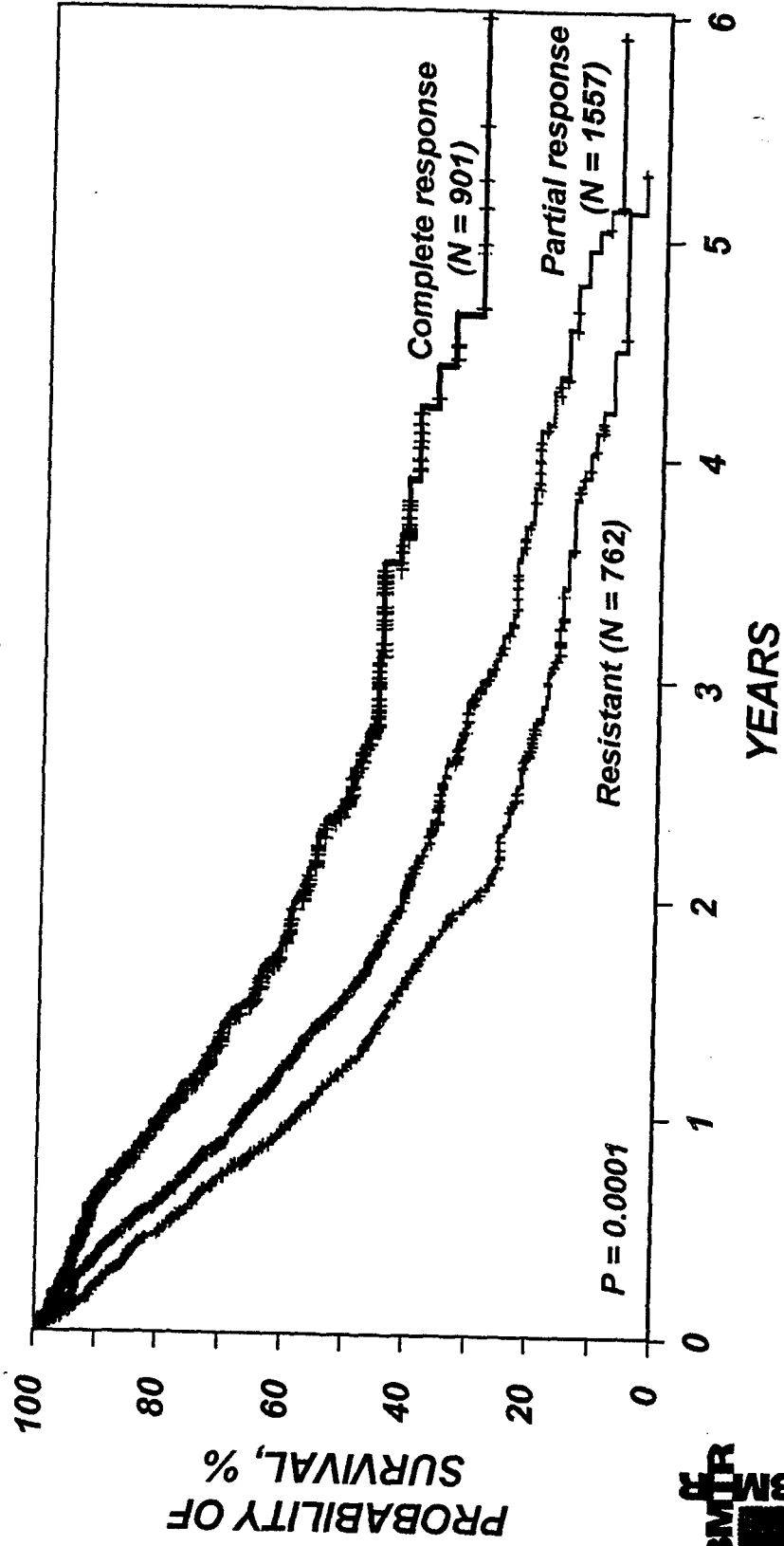
potential donors

welcome to BMT information

physicians corner

ask the expert

test your knowledge

diseases

about our sponsors

transplant topics

main
survey
glossary
q & a
disclaimer
related sites
text only

A cooperative effort of: National Marrow Donor Program
International Bone Marrow Transplant Registry
American Society of Blood and Marrow Transplantation

With funding support from: Department of Defense
Health Resources and Services Administration

Viewing Preference Text Only   With Images

BMTInformation

About our Sponsoring Organizations

National Marrow Donor Program

International Bone Marrow Transplant Registry/Autologous Blood and Marrow Transplant Registry North America

American Society of Blood and Marrow Transplantation

Health Resources and Services Administration

Department of the Army

National Institutes of Health

Welcome to BMTInformation at www.bmtinfo.org

BMTInformation

International Bone Marrow Transplant Registry/Autologous Blood and Marrow Transplant Registry N. America

The International Bone Marrow Transplant Registry (IBMTR) and the Autologous Blood and Marrow Transplant Registry of North America (ABMTR) are voluntary organizations of more than 400 institutions in 47 countries that submit data on their allogeneic and autologous blood and marrow transplant recipients to the IBMTR/ABMTR Statistical Center at the Medical College of Wisconsin in Milwaukee. The IBMTR, established in 1972, and the ABMTR, established in 1990, maintain databases of comprehensive clinical information for >50,000 transplant recipients. The information gathered by the IBMTR and ABMTR is used to identify trends in transplant use and outcome, to guide physicians and patients making treatment choices and for formal scientific studies of issues pertinent to improving transplant outcome. The IBMTR and ABMTR are entirely voluntary, non-profit organizations and represent a unique example of international cooperation that has greatly benefited the field of transplantation and cancer treatment.

Mission of the IBMTR and ABMTR

1. Maintain a Statistical Center for the collection, organization, and analysis of comprehensive clinical data on recipients of blood and marrow transplant recipients (the IBMTR collects data on allogeneic transplants, the ABMTR on autologous transplants);
2. Conduct studies addressing important issues in blood and marrow transplantation and cancer treatment;
3. Disseminates results of clinically relevant analyses by a variety of media to transplant centers and to the medical profession for the earliest possible benefit to patients;
4. Serves as resource of information on transplantation for patients, physicians and other individuals and organizations involved in health care.

For more information, visit the IBMTR/ABMTR website.

Welcome to BMTInformation at www.bmtinfo.org

BMTInformation

Potential Donors | Ask the Expert | Diseases | Transplant Topics | **About our Sponsors** | Test your Knowledge |
Physician's Corner
Main | Survey | Glossary | Q & A | Disclaimer | Related Sites | View With Images

---

Department of the Army

Partial funding support for this site has been provided by the Department of the Army (Grant DAMD17-95-I-5002). The content of this site does not necessarily reflect the position or the policy of the Department of the Army.

Potential Donors | Ask the Expert | Diseases | Transplant Topics | **About our Sponsors** | Test your Knowledge |
Physician's Corner
Main | Survey | Glossary | Q & A | Disclaimer | Related Sites | Text Only

Welcome to BMTInformation at www.bmtinfo.org

BMTInformation

Diseases Treated by Stem Cell Transplants

While there are many diseases that may be successfully treated by a bone marrow transplant, the list below highlights some of the diseases for which bone marrow transplant is most commonly considered. Please visit this site regularly as additional topics will be added to this list. Each description is available in both a technical and basic format. You may toggle your reading level at any time by clicking on the buttons at each subheading.

Articles

Autologous Blood and Bone Marrow Transplantation for BREAST CANCER

The Role of Blood and Bone Marrow Transplantation in CHRONIC MYELOGENOUS LEUKEMIA

Welcome to BMTInformation at www.bmtinfo.org

BMTInformation

Autologous Blood and Bone Marrow Transplantation for Breast Cancer

This text has been written at two levels: basic, for a general audience, and technical, for the reader with advanced knowledge of the topic.

Introduction
Basic | Technical

Current Data on Autotransplants
Basic | Technical

Clinical Trials
Basic | Technical

Published Papers

Welcome to BMTInformation at www.bmtinfo.org

BMTInformation

Autologous Blood and Bone Marrow Transplantation for Breast Cancer

Philip A. Rowlings, MBBS, M.S., FRACP, FRCPA
Assistant Scientific Director, IBMTR/ABMTR

Mary Horowitz, M.D., M.S.
Scientific Director, IBMTR/ABMTR

Introduction | Current Data | Clinical Trials | Published Papers

Introduction

Basic | **Technical**

Breast cancer is the second most common cause of cancer deaths in North America, and the American Cancer Society estimates that more than 180,000 new cases of breast cancer were diagnosed in 1996 (1). Many women with breast cancer are cured after local surgery with or without radiotherapy. Many others, however, have a recurrence of disease (either locally or at distant sites) after primary surgery or present with metastatic disease at diagnosis. Therefore, better treatments for patients with high-risk primary and advanced breast cancer continue to be investigated.

The role of high-dose chemotherapy with autologous hemopoietic stem cell support (autotransplant) as treatment for breast cancer remains controversial. The rationale for autotransplants is the dose-response relationship between many chemotherapy drugs and breast cancer, suggesting that increasing doses beyond the limits of bone marrow toxicity may increase cures. The controversy results from the high cost of autotransplants and the paucity of data comparing outcome with standard dose therapy. There have been legal disputes between patients wishing to undergo the procedure and third-party payers refusing to reimburse the costs. Some of these disputes have received extensive exposure.

Responding to the controversy, the U.S. Congress commissioned the General Accounting Office (GAO) to review this area. Its findings are summarized in a report entitled "Coverage of Autologous Bone Marrow Transplantation for Breast Cancer" (2). The GAO report made some recommendations about the financial and political issues governing dissemination of new technologies and health care in the United States. It produced no conclusions regarding use of autotransplants for patients with breast cancer. To determine the relative efficacy of autotransplants and standard therapy, several large trials sponsored by the National Cancer Institute are being conducted by the U.S. cooperative oncology groups. Accrual of patients into these trials is slower than expected, however, because patients and physicians are reluctant

to accept randomization to standard dose therapy. A careful review of the continued relevance and necessity of these trials was recently published (3).

Despite the controversy, use of autotransplants for patients with breast cancer has increased dramatically over the past 6 years. According to data reported to the Autologous Blood and Marrow Transplant Registry (ABMTR), which receives information on 40% to 50% of all transplants done in North America, about 3,500 autotransplants were done in 1995 for patients with breast cancer, making this disease the single most common indication for blood or marrow transplant of any kind (autologous or allogeneic).

References
1. Cancer Facts and Figures - 1996. Atlanta: American Cancer Society.
Return to article

2. United States General Accounting Office: Report to the Honorable Ron Wyden, U.S. Senate, Health Insurance "Coverage of Autologous Bone Marrow Transplantation for Breast Cancer." April 1996. GAO/HEHS-96-83.
Return to article

3. Gradishar WJ, Tallman MA, Abrams JS: High-dose chemotherapy of breast cancer. Ann Intern Med 125:599-604, 1996.
Return to article

Return to Top

Current Data on Autotransplants for Patients with Breast Cancer

Basic | **Technical**

Background

High-dose chemotherapy (either with or without radiation therapy) with autologous hematopoietic stem cell support (autotransplant) is increasingly used to treat breast cancer. According to data reported to the International Bone Marrow Transplant Registry (IBMTR) and the Autologous Blood and Marrow Transplant Registry (ABMTR) of North America, breast cancer is now the most common indication for hemopoietic stem cell transplant of any kind, either autologous or allogeneic. Published reports of autotransplants include relatively few patients, and substantial reporting biases are likely to exist (see selected list of references). Only one randomized study has been published. This study included ____ women with newly diagnosed metastatic breast cancer treated with either standard dose therapy or two courses of high-dose chemotherapy with stem cell support (1). This study showed a statistically significant advantage in both survival and disease-free survival for patients receiving autotransplants versus those receiving conventional dose chemotherapy. However, the 3-year survival in the autotransplant group was only ____%, suggesting that few women are cured with this approach. The study has been criticized because of its small sample size and choice of regimens. Until results of larger randomized trials or other carefully controlled clinical studies are available, most questions regarding the comparative efficacy of autotransplant versus standard dose therapy will remain unanswered. However, considerable data are available from the ABMTR and other sources regarding the safety and outcomes of high-dose treatment.

What Is the ABMTR?

The Autologous Blood and Marrow Transplant Registry of North America (ABMTR) is a voluntary organization of more than 200 transplant centers in the United States, Canada, and Central and South America. ABMTR centers report data on consecutive autotransplants to a Statistical Center at the Medical College of Wisconsin. The Statistical Center also collects data for allogeneic blood and bone marrow transplants (allotransplants) from centers participating in the International Bone Marrow Transplant Registry (IBMTR), a similar but independent organization of allotransplant centers worldwide. The ABMTR began collecting data in 1992. Data were collected retrospectively for patients receiving autotransplants between 1989 and 1992, and prospectively thereafter. Based on data collected by the Center for Disease Control Hospital Surveys (2,3), about half of autotransplants done in North America for all diseases are registered with the ABMTR. (Click here for a list of participating centers.)

Trends in Autotransplants and Mortality for Patients with Breast Cancer

Table 1 lists data reported to the ABMTR on almost 7,000 women receiving autotransplants for breast cancer. The number of autotransplants increased almost sixfold from 1989 to 1995. The disease stage at the time of transplant also changed significantly: while most autotransplants in 1989 were for metastatic disease, now more than half are done as adjuvant therapy for primary breast cancer (stages II, III and inflammatory disease). Stem cells collected from the blood are now the most common form of hematopoietic support. Most importantly, 100-day mortality decreased significantly from 18% in 1989-90 to 5% in 1995.

Table 1. Trends in autotransplants for breast cancer reported to the ABMTR 1989-1995.

Outcome in High-Risk Primary Breast Cancer

Kaplan-Meier estimates of survival after autotransplants for stages II, III and inflammatory breast cancer are shown in Figure 1. Three-year probabilities of survival after autotransplant are about 75% for women with stage II, 70% for women with stage III, and about 50% (range 40%-64%) for women with inflammatory breast cancer. Three-year probabilities of progression-free survival after autotransplant are about 65% for women with stage II, 60% for women with stage III, and 40% for women with inflammatory breast cancer. In 1995, the 100-day mortality rate was 4%.

Outcome in Metastatic Breast Cancer

Survival after autotransplant for metastatic breast cancer is predominantly determined by the responsiveness of the disease to standard dose therapy before transplant. Response is usually categorized as complete (disappearance of all known disease for 4 or more weeks), partial (a 50% or greater reduction in the size of measurable disease), or resistant (any response less than partial). Figures 1 and 2 show Kaplan-Meier estimates of survival after autotransplant for women with metastatic breast cancer according to disease-responsiveness before transplant. Three-year probabilities of survival after autotransplant are about 45% for women with complete response, 30% for women with partial response, and 15% for women with resistant metastatic breast cancer. Three-year probabilities of progression-free survival after autotransplant are about 30% for women with complete response, 15% for women with partial response and 5% for women with resistant metastatic breast cancer. In 1995, the 100-day mortality rate was 6%.

Autotransplants Versus Standard Dose Therapy for Breast Cancer

It is uncertain whether the results above are superior to those obtained in similar women using standard dose therapy. Comparing historical results with conventional therapy has caused several problems. Selection biases may occur since patients considered for autotransplant often have extensive medical evaluations before the procedure. This may detect occult metastatic disease in women with primary breast cancer and exclude from adjuvant transplant trials those patients who are likely to have poorer outcomes (4). Additionally, autotransplants are often restricted to women with good performance status and near-normal pulmonary, cardiac and renal function. Conversely, results of autotransplants might be expected to be worse compared to standard dose therapy when patients are treated as part of phase I studies with experimental and potentially toxic protocols. Meaningful comparisons of autotransplant versus standard dose therapy require careful adjustment for differences in factors related to the patient, the disease, and transplant, ideally in large randomized clinical trials.

References

1. Bezwoda WR, Seymour L, Dansey RD: High-dose chemotherapy with hematopoietic rescue as primary treatment for metastatic breast cancer: A randomized trial. Journal of Clinical Oncology 13:2483-2489, 1995.
Return to article

2. National Hospital Discharge Survey for 1990 and 1991. U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control. National Center for Health Statistics. Hospital Care Statistics Branch, 6525 Belcrest Road, Hyattsville, MD, 20782.
Return to article

3. Graves EJ: Detailed diagnoses and procedures, National Hospital Discharge Survey, 1989. Vital and Health Statistics - Series 13: Data from the National Health Survey. 108:1-236, 1991.
Return to article

4. Crump M, Goss PE, Prince M, Girouard C: Outcome of extensive evaluation before adjuvant therapy in women with breast cancer and 10 or more positive axillary lymph nodes. Journal of Clinical Oncology 14:66-69, 1996.
Return to article

Captions

Fig. 1. Probability of survival after autotransplants for breast cancer, 1989-1995.

Fig. 2. Probability of survival after autotransplants for metastatic breast cancer according to pretransplant chemosensitivity, 1989-1995.

Links to other resources of use to physicians and other health professionals caring for patients with breast cancer.

A comprehensive information service is provided by the NIH PDQ Search Service at http://cancernet.nci.nih.gov/trials/pdq_search.html

Return to Top

INDICATIONS FOR BLOOD AND MARROW TRANSPLANTATION IN NORTH AMERICA 1995
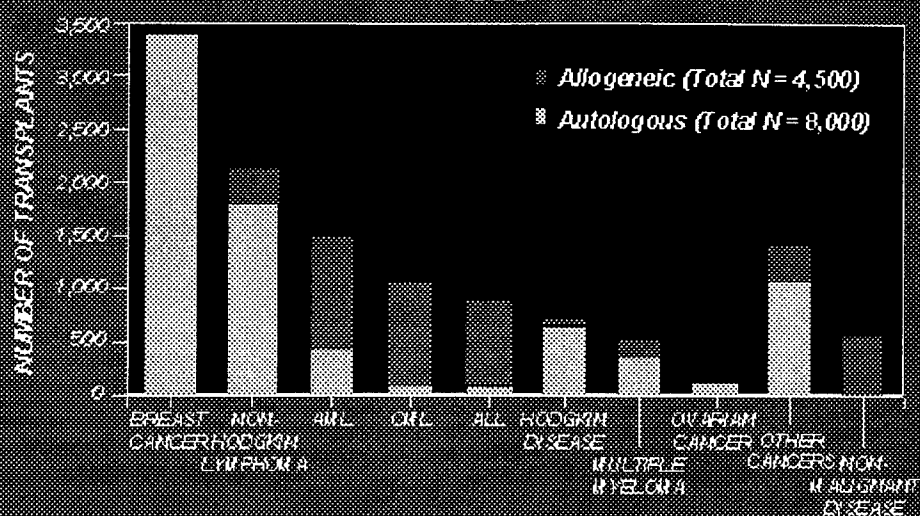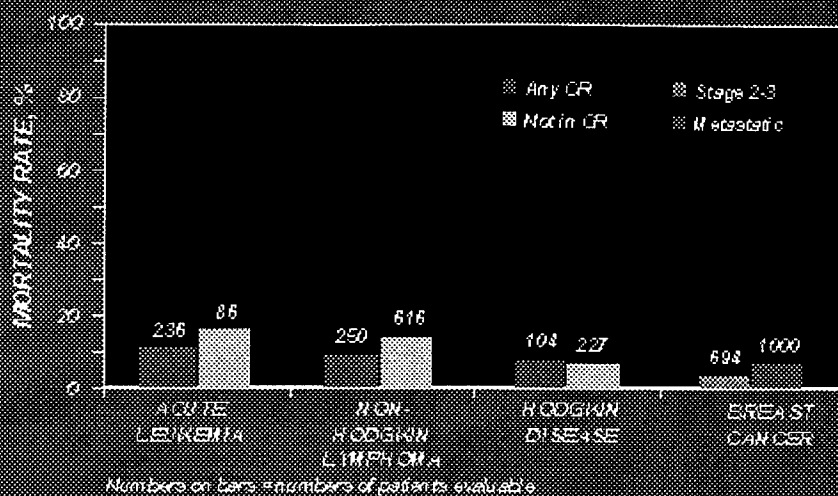
PROBABILITY OF SURVIVAL AFTER
AUTOTRANSPLANTS FOR BREAST CANCER
1989-1995
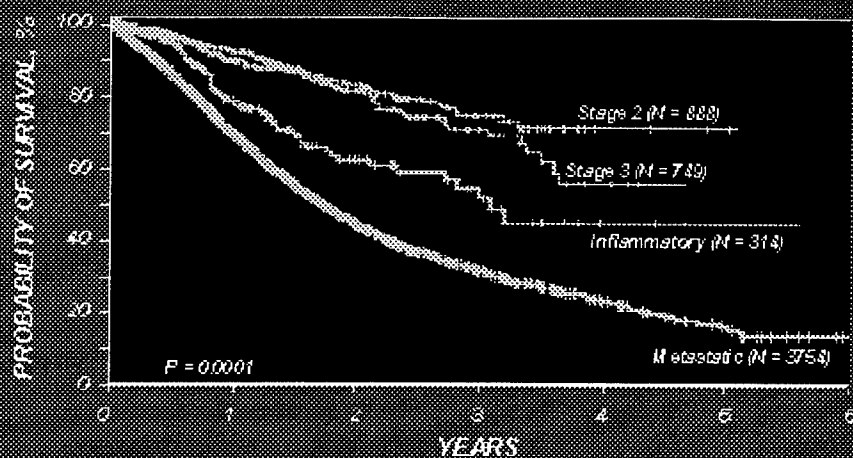
PROBABILITY OF SURVIVAL AFTER
AUTOTRANSPLANTS FOR METASTATIC BREAST CANCER
- Pretransplant Response to Chemotherapy -
1989-1995
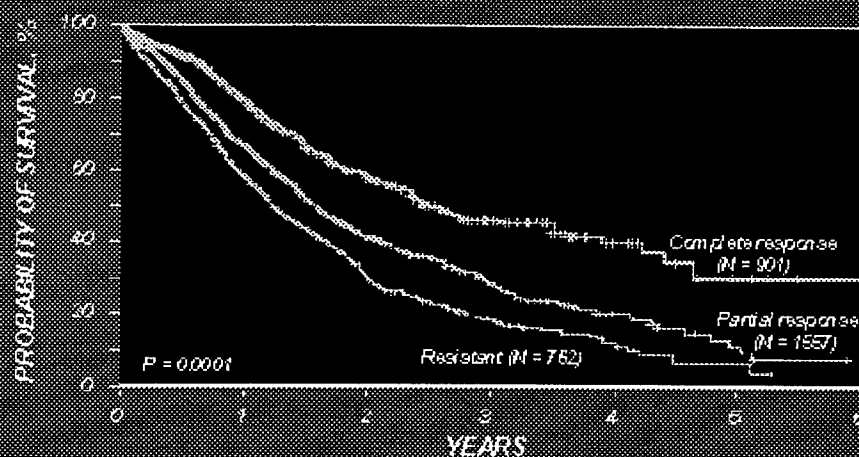
Clinical Trials

Basic | **Technical**

For details about enrolling a patient in one of these trials, contact the Chairpersons listed at the end of each trial summary. The details listed are correct as of the date given at the end of the title.

Additional Phase I and II trials are listed with the PDQ search service and are also conducted at individual transplant institutions.

Trials

- CLB-9082 INT-0163
- EST-2190 INT-0121
- E-PBT01 NCI-T90-0180D
- FHCRC-772.1 NCI-H94-0370
- S-9623 SWOG-9623

CLB-9082 INT-0163

NCI HIGH PRIORITY CLINICAL TRIAL --- Phase III Randomized Comparison of High-Dose Chemotherapy with Autologous Marrow and Peripheral Stem Cell Support vs Standard-Dose Chemotherapy Following Adjuvant Chemotherapy in Women with Stage II/IIIA Breast Cancer with at Least 10 Positive Axillary Nodes (Summary Last Modified 09/96)
STATUS: Active AGE RANGE: over 18

NCI-sponsored, NCI cooperative group program

OBJECTIVES:
I. Compare disease-free and overall survival of women with stage II/IIIA breast cancer randomized to receive high-dose cyclophosphamide/cisplatin/carmustine with autologous bone marrow/peripheral stem cell support plus chest wall irradiation vs. conventional doses of the same drugs plus chest wall irradiation, administered after 4 courses of adjuvant cyclophosphamide/doxorubicin/fluorouracil (CAF).

II. Compare the toxic effects of these 2 regimens.

PROTOCOL ENTRY CRITERIA:

--Disease Characteristics--

Histologically confirmed adenocarcinoma of the breast

Pathologically confirmed stage IIA, IIB, or IIIA (i.e., T1-3, N1-2, M0)

10 or more positive axillary nodes required

Absence of distant metastases, evidenced by:
    Negative bone scan
    Negative bilateral bone marrow aspirate/biopsy

Negative CT of head, chest, abdomen, pelvis

Hormone receptor status:
Any estrogen receptor (ER) or progesterone receptor (PR) status accepted, including unknown
Knowledge of ER and PR status desired

No bilateral breast cancer

--Prior/Concurrent Therapy--

Biologic therapy:
Not specified

Chemotherapy:
No prior chemotherapy

Endocrine therapy:
Not specified

Radiotherapy:
No prior radiotherapy

Surgery:
Radical or modified radical mastectomy or lumpectomy with level I/II axillary dissection required
Preferably within 2 weeks prior to initiating cyclophosphamide/doxorubicin/fluorouracil (CAF)
Not more than 8 weeks prior to initiating CAF (10 weeks with permission of the study chairman)
Negative resection margins required
Lymphatic and vascular involvement permitted

--Patient Characteristics--

Age:
Over 18
No upper limit, but over physiologic 50 expected to tolerate treatment less well

Sex:
Women only
Menopausal status:
Pre-, post-, or perimenopausal

Performance status:
CALGB 0 or 1
Karnofsky 80%-100%

Hematopoietic:
ANC at least 1,800/mL
Platelets at least 100,000/mL
Hemoglobin greater than 10 g/dL
Bone marrow cellularity at least 30%

Hepatic:
>Bilirubin not more than 1.5 times normal
>AST not more than 1.5 times normal

Renal:
>Creatinine less than 1.8 mg/dL
>BUN not more than 1.5 times normal

Cardiovascular:
>Left ventricular ejection fraction (LVEF) on MUGA at least 45% at rest and at least 5% increase with exercise (exercise test not required if LVEF is at least 55%)
>EKG required within 90 days prior to entry
>No uncontrolled or significant cardiovascular disease, i.e.:
>>No myocardial infarction within 1 year
>>No congestive heart failure

Pulmonary:
>FVC at least 60% of predicted
>FEV1 at least 60% of predicted
>DLCO at least 60% of predicted

Other:
>No previous or concomitant second malignancy except:
>>Curatively treated cervical cancer
>>Nonmelanomatous skin cancer

Negative viral titers, e.g.:
>HIV
>HBsAg
>Hepatitis C

No serious medical/psychiatric condition that would:
>Preclude protocol therapy
>Prevent informed consent

Companion quality-of-life study (CLB-9066) must be offered

PROTOCOL CHAIRPERSONS

William P. Peters, Chair Ph: 313-833-0715
>Director
>Barbara Ann Karmanos Cancer Institute
>110 East Warren Avenue
>Detroit, MI 48201-1379
>Cancer and Leukemia Group B Primary lead CLB-9082

James J. Vredenburgh, Co-Chair Ph: 919-684-6707
>Duke University Medical Center
>P.O. Box 3961
>Durham, NC 27710

Cancer and Leukemia Group B Primary lead CLB-9082

Elizabeth J. Shpall, Chair Ph: 303-372-9000
    University of Colorado Cancer Center
    Bone Marrow Transplant Program
    Campus Box B190
    4200 East Ninth Avenue
    Denver, CO 80262
    Southwest Oncology Group Secondary lead SWOG-9114

Michael Crump, Chair Ph: 416-340-3793
    Toronto General Hospital
    M-L 2-018
    200 Elizabeth Street
    Toronto, Ontario M5G 2C4
    Canada
    NCIC-Clinical Trials Group Secondary lead CAN-NCIC-MA13

Return to Clinical Trials

Return to Top

EST-2190 INT-0121

NCI HIGH PRIORITY CLINICAL TRIAL --- Phase III Randomized Study of Adjuvant CAF
(Cyclophosphamide/Doxorubicin/Fluorouracil) vs Adjuvant CAF Followed by Intensification with
High-Dose Cyclophosphamide/Thiotepa plus Autologous Stem Cell Rescue in Women with Stage I/III
Breast cancer at High Risk of Recurrence (Summary Last Modified 02/96)
STATUS: Active AGE RANGE: 15 to 60

SPONSORSHIP
NCI-sponsored, NCI cooperative group program

OBJECTIVES:
I. Compare sites and rates of recurrence, disease-free survival, overall survival, and toxicity of adjuvant
chemotherapy with CAF (cyclophosphamide, doxorubicin, fluorouracil) vs. adjuvant CAF followed by
marrow ablation with cyclophosphamide/thiotepa and autologous stem cell rescue in women with stage
II/III breast cancer and 10 or more positive lymph nodes.

II. Evaluate prospectively the incidence and degree of occult marrow contamination with breast cancer
cells at the time of study entry and following CAF chemotherapy by analyzing samples of marrow using a
panel of monoclonal antibodies specific for breast cancer.

III. Document the changes in psychosocial function that occur during treatment on either regimen, and
compare post-treatment recovery of psychosocial function.

IV. Establish a bank of paraffin-embedded tumor samples for future laboratory study.

PROTOCOL ENTRY CRITERIA:

--Disease Characteristics--

Biopsy-proven epithelial carcinoma of the breast with at least 10 involved lymph nodes

Stage II/III disease
    Synchronous bilateral breast cancer eligible provided primaries occurred within 6 weeks of each
    other
    Contralateral intraductal cancer eligible

The following conditions exclude:
    T4 disease
    Apocrine, adenoidcystic, or squamous carcinoma
    Inflammatory carcinoma of the breast
    Lesions fixed to skin or chest wall
    Peau d'orange skin changes
    Asynchronous bilateral infiltrating breast cancer

Radical or modified radical mastectomy or breast-sparing surgery with axillary dissection required within
12 weeks of entry
    Negative surgical margins required
    Type of procedure, number of nodes examined, number of positive nodes, and tumor size must be
    reported
    Breast-sparing surgery must have included wide excision (i.e., removal of gross tumor plus normal
    breast tissue)

Bone marrow aspirate, bilateral core biopsy, and bone scan must be negative for tumor
    Aspiration and biopsy not required for patients who received 1 or 2 courses of any
    doxorubicin-based chemotherapy prior to entry

Hormone receptor status:
    Estrogen and progesterone receptor status must be determined by either biochemical or
    immunohistochemical assays

--Prior/Concurrent Therapy--

Biologic therapy:
    No prior therapy with colony-stimulating factors for breast cancer

Chemotherapy:
    1 or 2 prior courses of any doxorubicin-based chemotherapy allowed provided documentation of
    treatment is available

Endocrine therapy:
    No prior hormonal therapy for breast cancer except up to 21 days of tamoxifen that is stopped
    prior to entry
    Prior postmenopausal estrogen therapy allowed but must be discontinued prior to entry

Radiotherapy:
    No prior radiotherapy

Postoperative radiotherapy required on study

Surgery:
Surgery completed no more than 12 weeks prior to entry
Surgery completed no more than 12 weeks prior to start of chemotherapy in patients who receive one or two courses of doxorubicin-based chemotherapy prior to randomization

--Patient Characteristics--

Age:
15 to 60

Sex:
Women only

Menopausal status:
Pre- or postmenopausal

Performance status:
ECOG 0 or 1

Hematopoietic:
(obtained within 2 weeks prior to entry)
WBC at least 4,000/mL
Platelets at least 100,000/mL

Hepatic:
(obtained within 2 weeks prior to entry)
Bilirubin no more than 1.2 times normal
AST (or ALT) no more than 1.2 times normal
Alkaline phosphatase no more than 1.2 times normal

Renal:
Not specified

Cardiovascular:
Left ventricular ejection fraction (by MUGA) at least 50% or equal to or greater than the lower limit of institutional normal
No prior angina pectoris requiring nitrate therapy
No myocardial infarction within 6 months
No uncontrolled congestive heart failure
No uncontrolled hypertension
No major ventricular arrhythmia

Pulmonary:
FEV1 at least 60% of predicted
DLCO (corrected) at least 60% of predicted
Lung volume at least 60%
Lung volume not required if uncorrected FEV1 and DLCO greater than 80%
No symptomatic obstructive or restrictive lung disease

Other:
No symptomatic CNS disease of any etiology
No insulin-dependent diabetes mellitus
No uncompensated major thyroid dysfunction
No uncompensated major adrenal dysfunction
No HIV positivity
No prior malignancy within 5 years except:
In situ breast cancer (lobular or ductal)
Inactive nonmelanomatous skin cancer
In situ cervical cancer
No pregnant or nursing women
Assessment of insurance coverage required

PROTOCOL CHAIRPERSONS

Martin Stuart Tallman, Chair Ph: 312-908-8697
Northwestern University Hematology/Oncology
Suite 700
233 East Erie Street
Chicago, IL 60611
Eastern Cooperative Oncology Group Primary lead EST-2190

William P. Vaughan, Chair Ph: 205-934-1908
Bone Marrow Transplantation Program
University of Alabama at Birmingham
541 Tinsley Harrison Tower
1900 University Boulevard
UAB Station
Birmingham, AL 35294-0006
Cancer and Leukemia Group B Secondary lead CLB-9496

Charles F. LeMaistre, Chair Ph: 210-593-3801
South Texas Cancer Institute
7700 Floyd Curl Drive
San Antonio, TX 78229
Southwest Oncology Group Secondary lead SWOG-9061

Return to Clinical Trials

Return to Top

E-PBT01 NCI-T90-0180D

NCI HIGH PRIORITY CLINICAL TRIAL --- Phase III Randomized Comparison of Conventional CMF Maintenance vs High-Dose Combination Chemotherapy plus Autologous Bone Marrow and Peripheral Stem Cell Rescue in Women with Metastatic Breast Cancer Responding to Conventional Induction Chemotherapy (Summary Last Modified 06/96)
STATUS: Active AGE RANGE: 18 to 60

NCI-sponsored, NCI cooperative group program

OBJECTIVES

I. Compare time to failure and overall survival of patients with metastatic breast cancer responding after 4-6 courses of conventional induction chemotherapy who are randomly assigned to 24 months of conventional maintenance chemotherapy with CMF (cyclophosphamide/methotrexate/fluorouracil) vs. high-dose chemotherapy with cyclophosphamide/thiotepa/carboplatin followed by autologous bone marrow and peripheral stem cell rescue.

II. Compare the toxicity of these 2 regimens.

III. Compare the financial costs of these 2 regimens.

IV. Evaluate the quality of life associated with these 2 treatments.

PROTOCOL ENTRY CRITERIA

--Disease Characteristics--

Histologically documented adenocarcinoma of the breast

Metastatic or recurrent disease
        No leptomeningeal or brain metastases
        Inflammatory breast cancer requires distant metastases
        Adequate hepatic function (see below) required with liver metastases
        Metastases to ipsilateral regional lymph nodes (supraclavicular or cervical) only may be treated by mastectomy or locoregional radiotherapy

Hormonal receptor status:
        Estrogen receptor (ER)-negative or unknown
        ER-positive (at least 10 fmol/mg cytosol protein) bone/soft tissue disease eligible only if progressed on at least 1 hormone manipulation in the adjuvant or metastatic setting
        ER-positive, visceral disease eligible without prior hormone therapy

Bidimensionally measurable or evaluable disease, as follows:
        Not irradiated or progressed since radiotherapy

Evaluable disease defined as:
        Blastic and mixed blastic/lytic lesions with no anticipated need for palliative radiotherapy during first 3 courses
        Pure osteolytic lesions
        Positive bone scan as only evidence of metastasis permitted provided patient has analgesic requirement or decreased performance status
                Evidence must be unequivocal if bone x-ray is negative
        Hepatic metastases greater than 2 cm on CT or MRI or of any size if biopsy-proven
        Abdominal or pelvic mass on CT or MRI
        Multinodular or confluent lung or skin metastases
        Cytologically positive pleural effusion

No large third-space fluid accumulation that cannot be drained

No large pericardial effusion

--Prior/Concurrent Therapy--

Biologic therapy:
    Not specified

Chemotherapy:
    One course of induction therapy as specified in the protocol allowed prior to entry
    No other chemotherapy for metastatic disease, except patient may have relapsed after primary
    treatment for stage IV disease by virtue of metastasis only to ipsilateral supraclavicular nodes
    At least 6 months between adjuvant chemotherapy and recurrence

Endocrine therapy:
    Prior hormone manipulation required for bone or visceral metastasis unless rapidly progressing

At least 4 weeks since or no benefit from oophorectomy for metastatic or recurrent disease

Radiotherapy:
    None to pelvic bones or lower spine
    No anticipated requirement for palliation during first 3 courses

Surgery:
    At least 2 weeks since major surgery

--Patient Characteristics--

Age:
    18 to 60

Sex:
    Women only

Menopausal status:
    Premenopausal or postmenopausal

Performance status:
    ECOG 0 or 1

Hematopoietic:
    ANC at least 1,500/mL
    Platelets at least 100,000/mL

Hepatic:
    Bilirubin not greater than 2.0 mg/dL
    AST/alkaline phosphatase not greater than 2 times normal
    If liver function compromised by metastatic disease:
        Bilirubin not greater than 5.0 mg/dL

AST not greater than 600 U/mL

Renal:
    After hydration:
        Creatinine not greater than 1.5 mg/dL and/or
        Creatinine clearance at least 60 mL/min

Cardiovascular:
    No significant cardiovascular disease, i.e.:
        No congestive heart failure
        No myocardial infarction within 3 months
        No arrhythmia requiring medication
        No poorly controlled hypertension (diastolic over 100 mm Hg)

Pulmonary:
    No significant non-neoplastic pulmonary disease

Other:
    No active infection
    No active peptic ulcer disease
    No brittle insulin-dependent diabetes mellitus
    No hospitalization for psychiatric illness, including severe depression or psychosis
    No current alcohol or drug abuse
    No pregnant or nursing women
    Not HIV seropositive and no clinical evidence of AIDS
    No active second malignancy within 10 years except:
        Curatively treated nonmelanomatous skin cancer
        In situ cervical carcinoma

PROTOCOL CHAIRPERSONS

Edward Allen Stadtmauer, Chair Ph: 215-662-7806
    University of Pennsylvania Cancer Center
    6 Penn Tower
    3400 Spruce Street
    Philadelphia, PA 19104
    Eastern Cooperative Oncology Group Primary lead E-PBT01

James N. Ingle, Chair Ph: 507-284-2511
    Mayo Clinic
    Division of Medical Oncology
    200 First Street Southwest
    Rochester, MN 55905
    North Central Cancer Treatment Group Secondary lead NCCTG-913201

Kenneth F. Mangan, Chair Ph: 215-707-2847
    Temple University Hospital
    Bone Marrow Transplant Program
    Department of Medicine
    3322 North Broad Street

Philadelphia, PA 19140
Southwest Oncology Group Secondary lead SWOG-9412

Edward Allen Stadtmauer, Chair Ph: 215-662-7806
University of Pennsylvania Cancer Center
6 Penn Tower
3400 Spruce Street
Philadelphia, PA 19104
Philadelphia Bone Marrow Transplant Group Secondary lead PBT-1

Return to Clinical Trials

Return to Top

FHCRC-772.1 NCI-H94-0370

Phase III Randomized Study of Autologous Bone Marrow vs G-CSF-Stimulated Peripheral Blood Stem Cell Transplantation for High-Risk Breast Carcinoma (Summary Last Modified 06/94)
STATUS: Active AGE RANGE: no greater than 65

SPONSORSHIP
NCI-sponsored, NCI grant supported

OBJECTIVES
I. Determine which stem cell source, autologous bone marrow (AuBM) or autologous peripheral blood stem cells (PBSC) mobilized with granulocyte colony-stimulating factor (G-CSF), results in more rapid engraftment in patients with high-risk or advanced breast carcinoma given post-transplant G-CSF.

II. Compare the rate and duration of infection, transfusion requirements, days of hospitalization, and rate of transplant-related complications between patients receiving PBSC vs. AuBM.

III. Compare the total cost of hospitalization when using PBSC vs. AuBM.

IV. Evaluate long-term engraftment in the two treatment groups.

V. Evaluate occult tumor cells in peripheral blood and marrow, and evaluate T-cell populations in PBSC collections.

PROTOCOL ENTRY CRITERIA

--Disease Characteristics--

High-risk breast carcinoma that has failed conventional therapy or has a greater than 50% chance for relapse, i.e.:
Stage II with more than 10 positive nodes
Stage III
Stage IV

No evidence of marrow involvement on biopsy

Marrow positive only by immunocytochemistry allowed

No rapidly progressing disease requiring immediate therapy

No carcinomatous meningitis or untreated CNS disease

Hormone receptor status:
    Not specified

--Prior/Concurrent Therapy--

Biologic therapy:
    Not specified

Chemotherapy:
    No more than 3 prior courses of myelosuppressive chemotherapy for metastatic disease

Endocrine therapy:
    Not specified

Radiotherapy:
    No prior pelvic irradiation

Surgery:
    Not specified

--Patient Characteristics--

Age:
    No greater than 65

Menopausal status:
    Not specified

Sex:
    Not specified

Performance status:
    Karnofsky 70%-100%

Hematopoietic:
    ANC at least 1,500/mL
    Platelets at least 150,000/mL
    Marrow cellularity at least 60% of normal
    No history of prolonged neutropenia (ANC below 500 for more than 30 days) after conventional-dose chemotherapy

Hepatic:
    Bilirubin no greater than 1.5 mg/dL

Renal:
>   Creatinine no greater than 1.5 mg/dL
>   No history of severe cyclophosphamide-induced hemorrhagic cystitis

Cardiovascular:
>   LVEF at least 45%

Other:
>   No HIV antibody
>   Willing to undergo multiple aphereses
>   Marrow available or patient willing to undergo marrow harvest

PROTOCOL CHAIRPERSONS

William I. Bensinger, Chair Ph: 206-667-4933
>   Fred Hutchinson Cancer Research Center
>   1124 Columbia Street
>   Seattle, WA 98104
>   Fred Hutchinson Cancer Research Center Primary lead FHCRC-772.1

Return to Clinical Trials

Return to Top

S-9623 SWOG-9623

Phase III Randomized Study of Intensive Sequential Doxorubicin, Paclitaxel, and Cyclophosphamide vs Doxorubicin/Cyclophosphamide Followed by STAMP I or STAMP V Combination Chemotherapy with Autologous Stem Cell Rescue in Women with Primary Breast Cancer and 4-9 Involved Axillary Lymph Nodes (Summary Last Modified 08/96)
STATUS: Active AGE RANGE: adult

NCI-sponsored, NCI cooperative group program

OBJECTIVES
I. Compare disease-free and overall survival following intensive sequential chemotherapy with doxorubicin, paclitaxel, and cyclophosphamide versus standard dose doxorubicin/cyclophosphamide followed by high-dose STAMP I (cyclophosphamide/cisplatin/carmustine) or STAMP V (cyclophosphamide/carboplatin/thiotepa) and autologous peripheral blood progenitor cell or bone marrow rescue in women with operable breast cancer and 4-9 positive axillary lymph nodes.

II. Compare the toxic effects associated with these regimens.

PROTOCOL ENTRY CRITERIA

--Disease Characteristics--

>   Histologically confirmed adenocarcinoma of the breast with 4-9 histologically involved axillary lymph nodes

No known T4, N3, or M1 disease

Prior breast-sparing surgery or modified radical mastectomy plus axillary lymph node dissection required
> Surgical margins negative for invasive or noninvasive ductal carcinoma
> At least 10 nodes sampled
> No more than 12 weeks since definitive surgery

Synchronous bilateral breast carcinoma eligible, provided:
> One breast meets the eligibility criteria
> Other breast has fewer than 10 involved nodes and is not N3 or T4

Hormone receptor status:
> Not specified

--Prior/Concurrent Therapy--

Biologic therapy:
> Not specified

Chemotherapy:
> No prior chemotherapy

Endocrine therapy:
> Not specified

Radiotherapy:
> No prior radiotherapy to the breast

Surgery:
> See Disease Characteristics

--Patient Characteristics--

Age:
> Adult

Sex:
> Women only

Menopausal status:
> Any status

Performance status:
> SWOG 0 or 1

Hematopoietic:
> WBC at least 3,000/mL
> ANC at least 1,000/mL
> Platelets at least 100,000/mL

Hepatic:
>   Bilirubin no greater than 1.5 times normal
>   AST no greater than 1.5 times normal

Renal:
>   Creatinine clearance at least 60 mL/min

Cardiovascular:
>   Left ventricular ejection fraction at rest at least 45% by MUGA
>   EKG abnormalities require patient clearance by cardiologist
>   No uncontrolled or significant cardiac disease
>   No congestive heart failure
>   No second- or third-degree heart block or other serious cardiac conduction abnormality
>   No atrial or ventricular arrhythmia
>   No requirement for medication known to affect cardiac conduction unless:
>> Given for reasons other than heart failure or arrhythmia
>> Patient cleared by a cardiologist

Pulmonary:
>   FVC and FEV1 at least 60% of predicted
>   DLCO at least 60%

Other:
>   No HIV antibody
>   Known HBsAg and hepatitis C status required
>   No serious medical or psychiatric illness that precludes informed consent or study participation
>   No second malignancy within 5 years except adequately treated:
>> Nonmelanomatous skin cancer
>> In situ cervical cancer
>   No pregnant or nursing women
>   Effective contraception required of fertile women

PROTOCOL CHAIRPERSONS

Scott I. Bearman, Chair Ph: 303-372-9000
>   University of Colorado Cancer Center
>   Box B-190
>   4200 East Ninth Avenue
>   Denver, CO 80262
>   Southwest Oncology Group Primary lead S-9623

Clifford A. Hudis, Chair Ph: 212-639-6483
>   Memorial Sloan-Kettering Cancer Center
>   Box # 206
>   1275 York Avenue
>   New York, NY 10021
>   Cancer and Leukemia Group B Secondary lead CLB-S9623

William Costin Wood, Chair Ph: 404-248-3301
Emory University Hospital
Suite B206
1365 Clifton Road NE
Atlanta, GA 30322
Eastern Cooperative Oncology Group Secondary lead E-S9623

Return to Clinical Trials

Return to Top

Potential Donors | Ask the Expert | **Diseases** | Transplant Topics | About our Sponsors | Test your Knowledge |
Physician's Corner
Main | Survey | Glossary | Q & A | Disclaimer | Related Sites | Text Only

Welcome to BMTInformation at www.bmtinfo.org

BMTInformation

Autologous Blood and Bone Marrow Transplantation for Breast Cancer

Philip A. Rowlings, MBBS, M.S., FRACP, FRCPA
Assistant Scientific Director, IBMTR/ABMTR

Mary Horowitz, M.D., M.S.
Scientific Director, IBMTR/ABMTR

Introduction | Current Data | Clinical Trials | Published Papers

Introduction

Basic | Technical

Breast cancer is the second most common cause of cancer deaths in North America. The American Cancer Society estimates that more than 180,000 new cases of breast cancer were diagnosed in 1996 (1). Fortunately, many women are cured of their disease through surgery with or without radiation therapy, chemotherapy, or hormone treatments after surgery. Unfortunately, the disease returns in many women, either at the same or another site. Still other women have metastasis—disease outside the breast and lymph nodes—at the time of diagnosis, which cannot be cured with surgery. So, scientists continue to look for effective treatments for women with recurrent or high-risk breast cancer.

A treatment used currently for women with recurrent breast cancer is high-dose chemotherapy followed by transplantation of the patient's own bone marrow or blood cells. This is called autologous transplant or *autotransplant*. This treatment, however, is controversial for patients with breast cancer. The therapy is expensive, and there is little information comparing the results of autotransplant with the results of standard chemotherapy. This controversy about autotransplants has caused legal problems between patients wishing to have the treatment and insurance companies refusing to pay for this treatment.

In response to the controversy, the U.S. Congress asked the General Accounting Office to write a report about the treatment. This report is entitled "Coverage of Autologous Bone Marrow Transplantation for Breast Cancer" (2). The report analyzed the financial and political issues that affect the use of new technologies for health care in the United States. But this report did not reach any conclusions about the use of autotransplants for patients with breast cancer.

The National Cancer Institute is trying to compare the results of autotransplants with those of standard therapy by sponsoring several large clinical trials in cancer centers throughout the United States. In these

trials, patients are randomly assigned to different types of treatment and their outcomes are compared. Patients enrolling in these trials have a 50-50 chance of receiving a transplant. Randomized trials are the best way to determine whether one treatment is better than another. These trials are especially appropriate in evaluating treatments such as autotransplants for breast cancer, in which the true benefit is unknown. Several studies show that patients treated in clinical trials have better outcomes than those treated outside of trials, regardless of which treatment they receive. However, many patients and their physicians hesitate to get involved in these trials because they do not want to be assigned to the standard therapy (3).

Despite the controversy, the use of autotransplants for patients with breast cancer has greatly increased in the past 6 years. Data reported to the Autologous Blood and Marrow Transplant Registry (ABMTR) show that about 3,500 autotransplants were done in 1995 for patients with breast cancer.

References

1. Cancer Facts and Figures - 1996. American Cancer Society.
Return to article

2. Unites States General Accounting Office: Report to the Honorable Ron Wyden, U.S. Senate, Health Insurance "Coverage of Autologous Bone Marrow Transplantation for Breast Cancer." April 1996. GAO/HEHS-96-83.
Return to article

3. Gradishar WJ, Tallman MS, Abrams JS. High-dose chemotherapy of breast cancer. Ann Intern Med 125:599-604, 1996.
Return to article

Return to Top

Current Data

Background

Basic | Technical

High-dose chemotherapy combined with autotransplant is being used more and more often to treat breast cancer in women who have a high risk of their breast cancer continuing or recurring. Two organizations keeping track of information about transplants for breast cancer and other diseases are the International Bone Marrow Transplant Registry (IBMTR) and the Autologous Blood and Marrow Transplant Registry (ABMTR) of North America. According to data from these organizations, breast cancer is now the most common reason for blood cell or bone marrow transplantation.

Currently, most reports published about autotransplants include only a few patients and do not compare results with standard chemotherapy. Only one small study has been published of women with metastatic breast cancer treated with either standard dose or high-dose chemotherapy (1). This study included only women with newly diagnosed metastatic breast cancer. It showed a longer survival period for patients who had autotransplants. However, the results of larger trials and other clinical studies are not yet available. Until these results are published, most questions about the advantages of autotransplant cannot be answered. In the meantime, data about the safety of autotransplants and the outcome of patients

having this treatment are available from the ABMTR and other sources.

What Is the ABMTR?

The Autologous Blood and Marrow Transplant Registry (ABMTR) of North America is an organization of more than 200 transplant institutions in the United States, Canada, and Central and South America. These institutions report data about autotransplants to a Statistical Center at the Medical College of Wisconsin. The ABMTR began to collect data in 1992. About half of the autotransplants done in North America for patients with all diseases are registered with the ABMTR (2,3). (Click here for a list of participating centers.)

Trends in Autotransplants and Deaths for Patients with Breast Cancer

From 1989 to 1995, the number of autotransplants increased by almost six times. At first, autotransplants were done primarily for patients with metastatic disease. More recently, autotransplants have been done more often for women with primary breast cancer (stage II, stage III, and inflammatory disease). Most important, the percentage of patients who had died by 100 days after treatment decreased from 18% (1989) to 5% (1995).

Outcome for Patients with High-Risk Primary Breast Cancer

Figure 1 shows the estimates of survival time after autotransplant in patients with stage II, stage III, and inflammatory breast cancer. The chances that a woman with stage II breast cancer will still be living 3 years after autotransplant are about 75%. For women with stage III breast cancer, the chance is 70%. For those with inflammatory breast cancer, the chance is about 50%.

For a woman with stage II breast cancer, the chance that she will still be living *and her disease will not have progressed* 3 years after autotransplant is about 65%. For women with stage III breast cancer, this chance is 60%. For those with inflammatory breast cancer, the chance is 40%. In 1995, only 4% of patients undergoing autotransplant had died by 100 days after treatment.

Outcome for Patients with Metastatic Breast Cancer

A patient's survival after autotransplant for metastatic breast cancer is often predicted by how the disease responds to standard dose chemotherapy before the patient has the transplant (Fig. 1, Fig. 2). The way that breast cancer responds to standard dose therapy is classified in one of three ways: 1) complete disappearance, 2) partial disappearance (in which the size of disease is reduced by at least half), or 3) resistant. For a woman whose metastatic cancer disappears completely after standard chemotherapy, the chance that she will still be alive 3 years after having an autotransplant is about 45%. For women with only partial disappearance after standard dose chemotherapy, the chance of surviving 3 years after autotransplant is about 30%. For those with resistant metastatic cancer, the chance of surviving 3 years is about 15%.

For a woman whose metastatic cancer disappears completely after standard chemotherapy, the chance that she will still be living *and her disease will not have progressed* 3 years after autotransplant is about 30%. For women with partial disappearance, this chance is about 15%. For those with resistant metastatic breast cancer, this chance is about 5%. In 1995, 6% of patients with metastatic breast cancer who underwent autotransplant died by 100 days after treatment.

Autotransplants Versus Standard Dose Therapy for Patients with Breast Cancer

Scientists are not certain whether the results reported for patients undergoing autotransplant are better than those reported for patients having standard dose therapy. Currently, comparing the results of these two treatments can cause several problems. A bias in the selection of patients for study may occur. This bias can happen because patients planning to have an autotransplant often undergo extensive medical tests before the procedure. These tests can detect hidden diseases and exclude from the study any patients who might have poor results (4). In addition, patients who undergo autotransplants are often chosen because their lungs, heart and kidneys are functioning well. These factors are likely to lead to better results.

If scientists are to compare the results of autotransplant and standard dose therapy in a useful way, they must analyze the data and carefully adjust it for factors that affect the patient, the disease, and the transplant. The best way to do this is in large randomized trials in which all patients are evaluated and followed carefully, regardless of the therapy they are assigned. Several studies suggest that people treated in randomized trials have better outcomes than people receiving the same treatment outside of trials.

References

1. Bezwoda WR, Seymour L, Dansey RD: High-dose chemotherapy with hematopoietic rescue as primary treatment for metastatic breast cancer: A randomized trial. Journal of Clinical Oncology 13:2483-2489, 1995.
Return to article

2. National Hospital Discharge Survey for 1990 and 1991. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control. National Center for Health Statistics. Hospital Care Statistics Branch, 6525 Belcrest Road, Hyattsville, MD, 20782.
Return to article

3. Graves EJ: Detailed diagnoses and procedures, National Hospital Discharge Survey, 1989. Vital and Health Statistics- Series 13: Data From the National Health Survey. 108:1-236, 1991.
Return to article

4. Crump M, Goss PE, Prince M, Girouard C: Outcome of extensive evaluation before adjuvant therapy in women with breast cancer and 10 or more positive axillary lymph nodes. Journal of Clinical Oncology. 14:66-69, 1996.
Return to article

Captions

Fig. 1. The probability of survival after autotransplant for patients with breast cancer, 1989-1995.

Fig. 2. The probability of survival after autotransplant for patients with metastatic breast cancer based on the sensitivity of the disease to standard chemotherapy before transplant, 1989-1995.

Links to other resources of use to physicians and other health professionals caring for patients with breast cancer.

A comprehensive information service is provided by the NIH PDQ Search Service at
http://cancernet.nci.nih.gov/trials/pdq_search.html

Return to Top

Clinical Trials

Basic | Technical

A *randomized clinical trial* (or Phase III trial) is an experiment done on human beings to evaluate the results of two or more therapies. Patients participating in the trials are randomly assigned to one of the therapies being studied. The outcomes of the patients receiving each type of treatment are then analyzed and compared.

Trial:

Comparison of high-dose chemotherapy and autotransplant versus standard dose chemotherapy in women with stage II and IIIA breast cancer and at least ten positive axillary nodes (NCI Clinical Trial #CLB-9082 INT-0163)

Description:

This Phase III trial is sponsored by the National Cancer Institute. The trial will compare the results of two groups of women undergoing treatment for stage II or IIIA breast cancer who have at least ten positive axillary nodes. The two treatments are:

1. High-dose chemotherapy with autotransplant and radiotherapy of the chest wall

2. Standard dose chemotherapy and radiotherapy of the chest wall after initial chemotherapy

Purposes:

To compare the survival rates of women with stage II or IIIA breast cancer who undergo these two treatments

To compare the toxic effects of these two treatments

Trial:

Randomized study of adjuvant chemotherapy versus adjuvant chemotherapy followed by high-dose chemotherapy and autotransplant in women with stage II or III breast cancer at high risk of recurrence (NCI Clinical Trial #EST-2190 INT-0121)

Description:

This Phase III trial is sponsored by the National Cancer Institute. The trial will compare the results of two types of treatment for women with stage II or stage III breast cancer who are at high risk of recurrence. The two treatments are:

1. Adjuvant chemotherapy
2. Adjuvant chemotherapy followed by high-dose chemotherapy and autotransplant

Purposes:

To compare the sites and rates of recurrent cancer, the survival rates, and toxicity of these two treatments in women with stage II or III breast cancer and ten or more positive lymph nodes

To evaluate the rate and degree of contamination of bone marrow by breast cancer cells at the time patients enter the study and after they undergo chemotherapy

To document the changes in psychosocial function in patients during treatment and compare their recovery of this function after treatment

To establish a bank of tumor samples for future laboratory study

---

Trial:

Comparison of conventional chemotherapy versus high-dose chemotherapy and autotransplant in women with metastatic breast cancer whose disease responds to conventional chemotherapy (NCI Clinical Trial #E-PBT01 NCI-T90-0180D)

Description:

This Phase III trial is sponsored by the National Cancer Institute. It will compare the results of two treatments in women with metastatic breast cancer whose disease responds to conventional chemotherapy. The two treatments are:
1. Conventional chemotherapy
2. High-dose chemotherapy and autotransplant

Purposes:

To compare the survival rates of patients with metastatic breast cancer whose disease responds to conventional chemotherapy and who undergo these two treatments

To compare the financial costs and toxicity of these two treatments

To evaluate the patients' quality of life associated with these two treatments

---

Trial:

Randomized study of autologous transplant versus transplantation of peripheral blood stem cells in patients with high-risk breast carcinoma (NCI Clinical Trial #FHCRC-772.1 NCI-H94-0370)

Description:

This Phase III trial is sponsored by the National Cancer Institute. The trial will determine which source of blood cells grafts faster in patients with high-risk or advanced breast cancer. The two sources of cells are:
1. Autologous bone marrow
2. Peripheral blood stem cells stimulated with granulocyte colony-stimulating factor (G-CSF)

Purposes:

To determine which of these two sources of stem cells leads to a faster graft in patients with high-risk or advanced breast cancer who are given G-CSF after undergoing transplant

To compare the rate and duration of infection, requirements for transfusion, the length of hospital stay, and the rate of complications between patients in these two groups

To compare the total cost of hospitalization between these two groups of patients

To evaluate long-term engraftment in the two treatment groups

To evaluate hidden tumor cells in peripheral blood and bone marrow, and to evaluate T-cell populations in collections of peripheral blood stem cells

---

Trial:

Randomized study of high-dose chemotherapy versus conventional chemotherapy followed by chemotherapy combined with autotransplant in women with primary breast cancer involving four to nine axillary nodes (NCI Clinical Trial #S-9623 SWOG-9623)

Description:

This Phase III trial is sponsored by the National Cancer Institute. It will compare the results of two treatments in women with primary breast cancer involving four to nine lymph nodes. The two treatments are:
1. Intensive sequential doses of three types of chemotherapy
2. Conventional chemotherapy followed by chemotherapy combined with autotransplant

Purposes:

To compare survival rates between women undergoing these two treatments

To compare the toxic effects associated with these treatments

Return to Top

Potential Donors | Ask the Expert | **Diseases** | Transplant Topics | About our Sponsors | Test your Knowledge |
Physician's Corner
Main | Survey | Glossary | Q & A | Disclaimer | Related Sites | Text Only

Welcome to BMTInformation at www.bmtinfo.org

BMTInformation

Selected list of recently published literature on autotransplants for patients with breast cancer by topics

Issues have been raised by the numerous published studies of small series of patients treated with autotransplants for breast cancer. Recently published data (authors, title and journal) are listed below according to topic.

A. Conditioning regimens used for autotransplant in women with Primary Breast Cancer
B. Conditioning regimens used for autotransplant in women with Recurrent or Metastatic Breast Cancer
C. Radiation therapy following autotransplant.
D. Immune modulation posttransplant to induce antitumor activity.
E. Detection of residual tumor cells in the stem cell source.
F. Purging of stem cell source to remove residual breast cancer cells.
G. Toxicity of autotransplants for breast cancer.
H. Safety of autotransplants for breast cancer.
I. Legal and financial issues.
J. Randomized trials involving autotransplants for breast cancer.
K. Prognostic factors in autotransplants for metastatic breast cancer.
L. Double (Tandem) autotransplants for breast cancer.
M. Pharmacokinetic monitoring in autotransplants for breast cancer.
N. Quality of life after autotransplants for breast cancer.
O. Hemopoetic stem cell sources for autotransplants for breast cancer.
P. Autotransplants as outpatients.
Q. Change in disease stage with extensive evaluation

A. Conditioning regimens used for autotransplant in women with Primary Breast Cancer

deMagalhaes-Silverman M. Rybka WB. Lembersky B. Bloom EJ. Lister J.
Pincus SM. Voloshin M. Wilson J. Ball ED.
High-dose cyclophosphamide, carboplatin, and etoposide with autologous
stem cell rescue in patients with breast cancer.
American Journal of Clinical Oncology. 19(2):169-73, 1996 Apr.

Broun ER. Sledge GW. Einhorn LH. Tricot GJ.
High-dose carboplatin and mitoxantrone with autologous bone marrow support
in the treatment of advanced breast cancer.
American Journal of Clinical Oncology. 16(1):9-13, 1993 Feb.

Spitzer TR. Cirenza E. McAfee S. Foelber R. Zarzin J. Cahill R.
Mazumder A.
Phase I-II trial of high-dose cyclophosphamide, carboplatin and autologous
bone marrow or peripheral blood stem cell rescue.
Bone Marrow Transplantation. 15(4):537-42, 1995 Apr.

Somlo G. Doroshow JH. Forman SJ. Leong LA. Margolin KA. Morgan RJ Jr.
Raschko JW. Akman SA. Ahn C. Nagasawa S. et al.
High-dose doxorubicin, etoposide, and cyclophosphamide with stem cell
reinfusion in patients with metastatic or high-risk primary breast cancer.
City of Hope Bone Marrow Oncology Team.
Cancer. 73(6):1678-85, 1994 Mar 15.

Somlo G. Doroshow JH. Forman SJ. Leong LA. Margolin KA. Morgan RJ Jr.
Raschko JW. Akman SA. Ahn C. Sniecinski I.
High-dose cisplatin, etoposide, and cyclophosphamide with autologous stem
cell reinfusion in patients with responsive metastatic or high-risk
primary breast cancer.
Cancer. 73(1):125-34, 1994 Jan 1.

de Graaf H. Willemse PH. de Vries EG. Sleijfer DT. Mulder PO.
van der Graaf WT. Smit Sibinga CT. van der Ploeg E. Dolsma WV. Mulder NH.
Department of Internal Medicine, University Hospital Groningen,
The Netherlands.
Intensive chemotherapy with autologous bone marrow transfusion as primary
treatment in women with breast cancer and more than five involved axillary lymph nodes.
European Journal of Cancer. 30A(2):150-3, 1994.

Mulder NH. Mulder PO. Sleijfer DT. Willemse PH. van der Ploeg E.
Dolsma WV. de Vries EG.
Department of Medical Oncology, University Hospital Groningen,
The Netherlands.
Induction chemotherapy and intensification with autologous bone marrow
reinfusion in patients with locally advanced and disseminated breast
cancer.
European Journal of Cancer. 29A(5):668-71, 1993.

Peters WP. Ross M. Vredenburgh JJ. Meisenberg B. Marks LB. Winer E.
Kurtzberg J. Bast RC Jr. Jones R. Shpall E. et al.
High-dose chemotherapy and autologous bone marrow support as consolidation
after standard-dose adjuvant therapy for high-risk primary breast cancer.
Journal of Clinical Oncology. 11(6):1132-43, 1993 Jun.

TMJ: a well-tolerated high-dose regimen for the adjuvant chemotherapy of
high risk breast cancer.
Journal of Medicine. 25(3-4):241-50, 1994.

Back to top

B. Conditioning regimens used for autotransplant in women with Recurrent or

Metastatic Breast Cancer

deMagalhaes-Silverman M. Rybka WB. Lembersky B. Bloom EJ. Lister J.
Pincus SM. Voloshin M. Wilson J. Ball ED.
High-dose cyclophosphamide, carboplatin, and etoposide with autologous
stem cell rescue in patients with breast cancer.
American Journal of Clinical Oncology. 19(2):169-73, 1996 Apr.

Kalaycioglu ME. Lichtin AE. Andresen SW. Tuason L. Bolwell BJ.
High-dose busulfan and cyclophosphamide followed by autologous bone marrow
transplantation and/or peripheral blood progenitor cell rescue for metastatic breast cancer.
American Journal of Clinical Oncology. 18(6):491-4, 1995 Dec.

Broun ER. Sledge GW. Einhorn LH. Tricot GJ.
High-dose carboplatin and mitoxantrone with autologous bone marrow support
in the treatment of advanced breast cancer.
American Journal of Clinical Oncology. 16(1):9-13, 1993 Feb.

Mulder NH. Dolsma WV. Mulder PO. De Vries EG. Willemse PH. Sleijfer
DT. Hospers GA. Van der Graaf WT.
Anticancer Research. 15(4):1565-8, 1995 Jul-Aug.

Lazarus HM. Gray R. Ciobanu N. Winter J. Weiner RS.
Phase I trial of high-dose melphalan, high-dose etoposide and autologous
bone marrow re-infusion in solid tumors: an Eastern Cooperative Oncology Group (ECOG) study.
Bone Marrow Transplantation. 14(3):443-8, 1994 Sep.

Weaver CH. Bensinger WI. Appelbaum FR. Lilleby K. Sandmaier B.
Brunvand M. Rowley S. Petersdorf S. Rivkin S. Gooley T. et al.
Phase I study of high-dose busulfan, melphalan and thiotepa with
autologous stem cell support in patients with refractory malignancies.
Bone Marrow Transplantation. 14(5):813-9, 1994 Nov.

Vaughan WP. Reed EC. Edwards B. Kessinger A.
High-dose cyclophosphamide, thiotepa and hydroxyurea with autologous
hematopoietic stem cell rescue: an effective consolidation chemotherapy
regimen for early metastatic breast cancer.
Bone Marrow Transplantation. 13(5):619-24, 1994 May.

Bowers C. Adkins D. Dunphy F. Harrison B. LeMaistre CF. Spitzer G.
Dose escalation of mitoxantrone given with thiotepa and autologous bone
marrow transplantation for metastatic breast cancer.
Bone Marrow Transplantation. 12(5):525-30, 1993 Nov.

Klumpp TR. Mangan KF. Glenn LD. Macdonald JS.
Phase II pilot study of high-dose busulfan and CY followed by autologous
BM or peripheral blood stem cell transplantation in patients with advanced
chemosensitive breast cancer.
Bone Marrow Transplantation. 11(4):337-9, 1993 Apr.

Somlo G. Doroshow JH. Forman SJ. Leong LA. Margolin KA. Morgan RJ Jr.
Raschko JW. Akman SA. Ahn C. Nagasawa S. et al.
High-dose doxorubicin, etoposide, and cyclophosphamide with stem cell
reinfusion in patients with metastatic or high-risk primary breast cancer.
City of Hope Bone Marrow Oncology Team.
Cancer. 73(6):1678-85, 1994 Mar 15.

Somlo G. Doroshow JH. Forman SJ. Leong LA. Margolin KA. Morgan RJ Jr.
Raschko JW. Akman SA. Ahn C. Sniecinski I.
High-dose cisplatin, etoposide, and cyclophosphamide with autologous stem
cell reinfusion in patients with responsive metastatic or high-risk
primary breast cancer.
Cancer. 73(1):125-34, 1994 Jan 1.

Schrier DM. Stemmer SM. Johnson T. Kasliwal R. Lear J. Matthes S.
Taffs S. Dufton C. Glenn SD. Butchko G. et al.
High-dose 90Y Mx-diethylenetriaminepentaacetic acid (DTPA)-BrE-3 and
autologous hematopoietic stem cell support (AHSCS) for the treatment of
advanced breast cancer: a phase I trial.
Cancer Research. 55(23 Suppl):5921s-5924s, 1995 Dec 1.

Mulder NH. Mulder PO. Sleijfer DT. Willemse PH. van der Ploeg E.
Dolsma WV. de Vries EG.
Department of Medical Oncology, University Hospital Groningen, The Netherlands.
Induction chemotherapy and intensification with autologous bone marrow
reinfusion in patients with locally advanced and disseminated breast cancer.
European Journal of Cancer. 29A(5):668-71, 1993.

Saez RA. Selby GB. Slease RB. Epstein RB. Mandanas RA. Confer DL.
Autologous bone marrow transplantation for metastatic breast cancer.
Journal - Oklahoma State Medical Association. 87(9):405-10, 1994 Sep.

Stemmer SM. Cagnoni PJ. Shpall EJ. Bearman SI. Matthes S. Dufton C.
Day T. Taffs S. Hami L. Martinez C. Purdy MH. Arron J. Jones RB.
High-dose paclitaxel, cyclophosphamide, and cisplatin with autologous
hematopoietic progenitor-cell support: a phase I trial.
Journal of Clinical Oncology. 14(5):1463-72, 1996 May.

Patrone F. Ballestrero A. Ferrando F. Brema F. Moraglio L. Valbonesi
M. Basta P. Ghio R. Gobbi M. Sessarego M.
Four-step high-dose sequential chemotherapy with double hematopoietic
progenitor-cell rescue for metastatic breast cancer.
Journal of Clinical Oncology. 13(4):840-6, 1995 Apr.

Ghalie R. Richman CM. Adler SS. Cobleigh MA. Korenblit AD. Manson SD.
McLeod BC. Taylor SG 4th. Valentino LA. Wolter J. et al.
Treatment of metastatic breast cancer with a split-course high-dose
chemotherapy regimen and autologous bone marrow transplantation.
Journal of Clinical Oncology. 12(2):342-6, 1994 Feb.

O'Brien ME. Talbot DC. Smith IE.
Carboplatin in the treatment of advanced breast cancer: a phase II study
using a pharmacokinetically guided dose schedule.
Journal of Clinical Oncology. 11(11):2112-7, 1993 Nov.

Williams SF. Gilewski T. Mick R. Bitran JD.
High-dose consolidation therapy with autologous stem-cell rescue in stage
IV breast cancer: follow-up report.
Journal of Clinical Oncology. 10(11):1743-7, 1992 Nov.

Antman K. Ayash L. Elias A. Wheeler C. Hunt M. Eder JP. Teicher BA.
Critchlow J. Bibbo J. Schnipper LE. et al.
A phase II study of high-dose cyclophosphamide, thiotepa, and carboplatin
with autologous marrow support in women with measurable advanced breast
cancer responding to standard-dose therapy [see comments].
Journal of Clinical Oncology. 10(1):102-10, 1992 Jan.

Fields KK. Elfenbein GJ. Perkins JB. Janssen WE. Ballester OF.
Hiemenz JW. Zorsky PE. Kronish LE. Foody MC.
High-dose ifosfamide/carboplatin/etoposide: maximum tolerable doses,
toxicities, and hematopoietic recovery after autologous stem cell reinfusion.
Seminars in Oncology. 21(5 Suppl 12):86-92, 1994 Oct.

Fields KK. Elfenbein GJ. Perkins JB. Hiemenz JW. Janssen WE. Zorsky
PE. Ballester OF. Kronish LE. Foody MC.
Two novel high-dose treatment regimens for metastatic breast
cancer--ifosfamide, carboplatin, plus etoposide and mitoxantrone plus
thiotepa: outcomes and toxicities.
Seminars in Oncology. 20(5 Suppl 6):59-66, 1993 Oct.

Return to top

C. Radiation therapy following autotransplant.

Marks LB. Rosner GL. Prosnitz LR. Ross M. Vredenburgh JJ. Peters WP.
The impact of conventional plus high dose chemotherapy with autologous
bone marrow transplantation on hematologic toxicity during subsequent
local-regional radiotherapy for breast cancer.
Cancer. 74(11):2964-71, 1994 Dec 1.

Shah AB. Hartsell WF. Ghalie R. Kaizer H.
Patterns of failure following bone marrow transplantation for metastatic
breast cancer: the role of consolidative local therapy.
International Journal of Radiation Oncology, Biology, Physics. 32(5):1433-8, 1995 Jul 30.

Mundt AJ. Sibley GS. Williams S. Rubin SJ. Heimann R. Halpern H. Weichselbaum RR.
Patterns of failure of complete responders following high-dose
chemotherapy and autologous bone marrow transplantation for metastatic
breast cancer: implications for the use of adjuvant radiation therapy
International Journal of Radiation Oncology, Biology, Physics. 30(1):151-60, 1994 Aug 30.

Marks LB. Halperin EC. Prosnitz LR. Ross M. Vredenburgh JJ. Rosner GL. Peters W.
Post-mastectomy radiotherapy following adjuvant chemotherapy and autologous bone marrow transplantation for breast cancer patients with greater than or equal to 10 positive axillary lymph nodes.
Cancer and Leukemia Group B
International Journal of Radiation Oncology, Biology, Physics.
23(5):1021-6, 1992.

Return to top

D. Immune modulation posttransplant to induce antitumor activity.

Yamasaki S. Kan N. Mise K. Harada T. Ichinose Y. Moriguchi Y. Kodama H. Satoh K. Ohgaki K. Tobe T.
Cellular interaction against autologous tumor cells between IL-2-cultured lymphocytes and fresh peripheral blood lymphocytes in patients with breast cancer given immuno-chemotherapy.
Biotherapy. 6(1):63-71, 1993.

Lazarus HM. Winton EF. Williams SF. Grinblatt D. Campion M. Cooper BW. Gunn H. Manfreda S. Isaacs RE.
Phase I multicenter trial of interleukin 6 therapy after autologous bone marrow transplantation in advanced breast cancer.
Bone Marrow Transplantation. 15(6):935-42, 1995 Jun.

Head JF. Elliott RL. McCoy JL.
Evaluation of lymphocyte immunity in breast cancer patients.
Breast Cancer Research & Treatment. 26(1):77-88, 1993.

McCulloch PG. MacIntyre A.
Effects of surgery on the generation of lymphokine-activated killer cells in patients with breast cancer.
British Journal of Surgery. 80(8):1005-7, 1993 Aug.

Baxevanis CN. Dedoussis GV. Papadopoulos NG. Missitzis I. Stathopoulos GP. Papamichail M.
Tumor specific cytolysis by tumor infiltrating lymphocytes in breast cancer.
Cancer. 74(4):1275-82, 1994 Aug 15.

Dadmarz R. Sgagias MK. Rosenberg SA. Schwartzentruber DJ.
CD4+ T lymphocytes infiltrating human breast cancer recognise autologous tumor in an MHC-class-II restricted fashion
Cancer Immunology, Immunotherapy. 40(1):1-9, 1995 Jan.

Kennedy MJ. Vogelsang GB. Jones RJ. Farmer ER. Hess AD. Altomonte V. Huelskamp AM. Davidson NE.
Phase I trial of interferon gamma to potentiate cyclosporine-induced graft-versus-host disease in women undergoing autologous bone marrow

transplantation for breast cancer
Journal of Clinical Oncology. 12(2):249-57, 1994 Feb.

Kennedy MJ. Vogelsang GB. Beveridge RA. Farmer ER. Altomonte V.
Huelskamp AM. Davidson NE.
Phase I trial of intravenous cyclosporine to induce graft-versus-host
disease in women undergoing autologous bone marrow transplantation for
breast cancer.
Journal of Clinical Oncology. 11(3):478-84, 1993 Mar.

Return to top

E. Detection of residual tumor cells in the stem cell source.

Brugger W. Bross KJ. Glatt M. Weber F. Mertelsmann R. Kanz L.
Mobilization of tumor cells and hematopoietic progenitor cells into
peripheral blood of patients with solid tumors.
Blood. 83(3):636-40, 1994 Feb 1.

Simpson SJ. Vachula M. Kennedy MJ. Kaizer H. Coon JS. Ghalie R.
Williams S. Van Epps D.
Detection of tumor cells in the bone marrow, peripheral blood, and
apheresis products of breast cancer patients using flow cytometry.
Experimental Hematology. 23(10):1062-8, 1995 Sep.

Fields KK. Elfenbein GJ. Trudeau WL. Perkins JB. Janssen WE.
Moscinski LC.
Clinical significance of bone marrow metastases as detected using the
polymerase chain reaction in patients with breast cancer undergoing
high-dose chemotherapy and autologous bone marrow transplantation.
Journal of Clinical Oncology. 14(6):1868-76, 1996 Jun.

Datta YH. Adams PT. Drobyski WR. Ethier SP. Terry VH. Roth MS.
Sensitive detection of occult breast cancer by the reverse-transcriptase
polymerase chain reaction.
Journal of Clinical Oncology. 12(3):475-82, 1994 Mar.

Return to top

F. Purging of stem cell source to remove residual breast cancer cells.

Shpall EJ. Stemmer SM. Hami L. Franklin WA. Shaw L. Bonner HS.
Bearman SI. Peters WP. Bast RC Jr. McCulloch W. et al.
Amifostine (WR-2721) shortens the engraftment period of
4-hydroperoxycyclophosphamide-purged bone marrow in breast cancer patients
receiving high-dose chemotherapy with autologous bone marrow support.
Blood. 83(11):3132-7, 1994 Jun 1.

Shpall EJ. Stemmer SM. Bearman SI. Myers S. Purdy M. Jones RB.

New strategies in marrow purging for breast cancer patients receiving
high-dose chemotherapy with autologous bone marrow transplantation.
Breast Cancer Research & Treatment. 26 Suppl:S19-23, 1993.

Myklebust AT. Godal A. Juell S. Pharo A. Fodstad O.
Comparison of two antibody-based methods for elimination of breast cancer
cells from human bone marrow.
Cancer Research. 54(1):209-14, 1994 Jan 1.

Kennedy MJ. Davis J. Passos-Coelho J. Noga SJ. Huelskamp AM. Ohly K.
Davidson NE.
Administration of human recombinant granulocyte colony-stimulating factor
(filgrastim) accelerates granulocyte recovery following high-dose
chemotherapy and autologous marrow transplantation with
4-hydroperoxycyclophosphamide-purged marrow in women with metastatic
breast cancer.
Cancer Research. 53(22):5424-8, 1993 Nov 15.

Dietzfelbinger HF. Kuhn D. Zafferani M. Hanauske AR. Rastetter JW.
Berdel WE.
Removal of breast cancer cells from bone marrow by in vitro purging with
ether lipids and cryopreservation.
Cancer Research. 53(16):3747-51, 1993 Aug 15.

Ingram SS. Samulski T. Dodge R. Prosnitz LR. Peters P. Vredenburgh J.
The effects of hyperthermia in bone marrow purging of breast cancer.
International Journal of Hyperthermia. 12(1):21-9, 1996 Jan-Feb.

Return to top

G. Toxicity of autotransplants for breast cancer

Stemmer SM. Stears JC. Burton BS. Jones RB. Simon JH.
White matter changes in patients with breast cancer treated with high-dose
chemotherapy and autologous bone marrow support.
Ajnr: American Journal of Neuroradiology. 15(7):1267-73, 1994 Aug.

Todd NW. Peters WP. Ost AH. Roggli VL. Piantadosi CA.
Pulmonary drug toxicity in patients with primary breast cancer treated
with high-dose combination chemotherapy and autologous bone marrow
transplantation.
American Review of Respiratory Disease. 147(5):1264-70, 1993 May.

Pittman KB. To LB. Bayly JL. Olweny CL. Abdi EA. Carter ML. Malycha
P. Gill PG. Walsh J. Ward GG. et al.
Non-haematological toxicity limiting the application of sequential high
dose chemotherapy in patients with advanced breast cancer.
Bone Marrow Transplantation. 10(6):535-40, 1992 Dec.

Marks LB. Rosner GL. Prosnitz LR. Ross M. Vredenburgh JJ. Peters WP.

The impact of conventional plus high dose chemotherapy with autologous
bone marrow transplantation on hematologic toxicity during subsequent
local-regional radiotherapy for breast cancer.
Cancer. 74(11):2964-71, 1994 Dec 1.

Lewkow LM. Hooker JL. Movahed A.
Cardiac complications of intensive dose mitoxantrone and cyclophosphamide
with autologous bone marrow transplantation in metastatic breast cancer.
International Journal of Cardiology. 34(3):273-6, 1992 Mar.

Patz EF Jr. Peters WP. Goodman PC.
Pulmonary drug toxicity following high-dose chemotherapy with autologous
bone marrow transplantation: CT findings in 20 cases.
Journal of Thoracic Imaging. 9(2):129-34, 1994 Spring.

Khawly JA. Rubin P. Petros W. Peters WP. Jaffe GJ.
Retinopathy and optic neuropathy in bone marrow transplantation for breast cancer.
Ophthalmology. 103(1):87-95, 1996 Jan.

Return to top

H. Safety of autotransplants for breast cancer

Holland HK. Dix SP. Geller RB. Devine SM. Heffner LT. Connaghan DG.
Hillyer CD. Hughes LL. Miller RL. Moore MR. Winton EF. Wingard JR.
Minimal toxicity and mortality in high-risk breast cancer patients
receiving high-dose cyclophosphamide, thiotepa, and carboplatin plus
autologous marrow/stem-cell transplantation and comprehensive supportive care.
Journal of Clinical Oncology. 14(4):1156-64, 1996 Apr.

Return to top

I. Legal and financial issues

Wynstra NA.
Breast cancer. Selected legal issues.
Cancer. 74(1 Suppl):491-511, 1994 Jul 1.

Hillner BE. Smith TJ. Desch CE.
Efficacy and cost-effectiveness of autologous bone marrow transplantation
in metastatic breast cancer. Estimates using decision analysis while
awaiting clinical trial results.
JAMA. 267(15):2055-61, 1992 Apr 15.

Eddy DM.
High-dose chemotherapy with autologous bone marrow transplantation for the
treatment of metastatic breast cancer.
Journal of Clinical Oncology. 10(4):657-70, 1992 Apr.

Peters WP. Rogers MC.
Variation in approval by insurance companies of coverage for autologous
bone marrow transplantation for breast cancer.
New England Journal of Medicine. 330(7):473-7, 1994 Feb 17.

Cutler CM. Udvarhelyi IS. Winkenwerder W.
Variations in insurance coverage for autologous bone marrow
transplantation for breast cancer.
New England Journal of Medicine. 331(5):329-30, 1994 Aug 4.

Erban JK.
Variations in insurance coverage for autologous bone marrow
transplantation for breast cancer
New England Journal of Medicine.
331(5):330, 1994 Aug 4.

Templeton KM.
Variations in insurance coverage for autologous bone marrow
transplantation for breast cancer.
New England Journal of Medicine.
331(5):330, 1994 Aug 4.

Wingard JR.
Variations in insurance coverage for autologous bone marrow
transplantation for breast cancer.
New England Journal of Medicine. 331(5):330, 1994 Aug 4.

Krause KJ.
Variations in insurance coverage for autologous bone marrow
transplantation for breast cancer.
New England Journal of Medicine.
331(5):330, 1994 Aug 4.

Khanna V.
Variations in insurance coverage for autologous bone marrow
transplantation for breast cancer.
New England Journal of Medicine.
331(5):330-1, 1994 Aug 4.

Return to top

J. Randomized trials involving autotransplants for breast cancer

Bezwoda WR. Seymour L. Dansey RD.
High-dose chemotherapy with hematopoietic rescue as primary treatment for
metastatic breast cancer: a randomized trial.
Journal of Clinical Oncology. 13(10):2483-9, 1995 Oct.

Rutqvist LE.
Randomized adjuvant breast cancer trials in Sweden.

Cancer. 74(3 Suppl):1156-9, 1994 Aug 1.

Osborne CK.
Current trials and future directions of the Southwest Oncology Group
Breast Cancer Committee.
Cancer. 74(3 Suppl):1135-8, 1994 Aug 1.

Wood WC.
Current trials and future directions of the Eastern Cooperative Oncology
Group Breast Cancer Committee.
Cancer. 74(3 Suppl):1132-4, 1994 Aug 1.

Hurd DD. Peters WP.
Randomized, comparative study of high-dose (with autologous bone marrow
support) versus low-dose cyclophosphamide, cisplatin, and carmustine as
consolidation to adjuvant cyclophosphamide, doxorubicin, and fluorouracil
for patients with operable stage II or III breast cancer involving 10 or
more axillary lymph nodes (CALGB Protocol 9082). Cancer and Leukemia Group B.
Monographs - National Cancer Institute. (19):41-4, 1995.

Return to top

K. Prognostic factors in autransplants for metastatic breast cancer

Rowlings PA. Antman KS. Horowitz MM. Williams SF. Lazarus HM. Fields KK. Pelz CJ.
Sobocinski KA. Armitage JO. for the Breast Cancer Working Committee of the Autologous
Blood and Marrow Transplant Registry-North America.
Prognostic factors in autotransplants for metastatic breast cancer.
Blood. 88(10): 618a, abstract 2459, 1995 Nov 15.

Dunphy FR. Spitzer G. Fornoff JE. Yau JC. Huan SD. Dicke KA. Buzdar
AU. Hortobagyi GN.
Factors predicting long-term survival for metastatic breast cancer
patients treated with high-dose chemotherapy and bone marrow support
Cancer. 73(8):2157-67, 1994 Apr 15.

Ayash LJ. Wheeler C. Fairclough D. Schwartz G. Reich E. Warren D.
Schnipper L. Antman K. Frei E 3rd. Elias A.
Prognostic factors for prolonged progression-free survival with high-dose
chemotherapy with autologous stem-cell support for advanced breast cancer.
Journal of Clinical Oncology. 13(8):2043-9, 1995 Aug.

Return to top

L. Double (Tandem) autotransplants for breast cancer

Broun ER. Sridhara R. Sledge GW. Loesch D. Kneebone PH. Hanna M.
Hromas R. Cornetta K. Einhorn LH.
Tandem autotransplantation for the treatment of metastatic breast cancer.

Journal of Clinical Oncology. 13(8):2050-5, 1995 Aug.

Ayash LJ. Elias A. Wheeler C. Reich E. Schwartz G. Mazanet R. Tepler
I. Warren D. Lynch C. Gonin R. et al.
Double dose-intensive chemotherapy with autologous marrow and
peripheral-blood progenitor-cell support for metastatic breast cancer: a
feasibility study.
Journal of Clinical Oncology. 12(1):37-44, 1994 Jan.

Bitran JD. Samuels B. Klein l. Hanauer S. Johnson L. Martinec J. Harris E. Kempler J. White W.
Tandem high-dose chemotherapy supported by hemapoietic progenitor cells yields prolonged
survival in stage IV breast cancer.
Bone Marrow Transplantation. 17; 157-162, 1996

Return to top

M. Pharmacokinetic monitoring in autotransplants for breast cancer

Jones RB. Matthes S. Dufton C. Bearman SI. Stemmer SM. Meyers S. Shpall EJ.
Pharmacokinetic/pharmacodynamic interactions of intensive
cyclophosphamide, cisplatin, and BCNU in patients with breast cancer.
Breast Cancer Research & Treatment. 26 Suppl:S11-7, 1993.

Chen TL. Passos-Coelho JL. Noe DA. Kennedy MJ. Black KC. Colvin OM. Grochow LB.
Nonlinear pharmacokinetics of cyclophosphamide in patients with metastatic
breast cancer receiving high-dose chemotherapy followed by autologous bone
marrow transplantation
Cancer Research. 55(4):810-6, 1995 Feb 15.

O'Brien ME. Talbot DC. Smith IE.
Carboplatin in the treatment of advanced breast cancer: a phase II study
using a pharmacokinetically guided dose schedule.
Journal of Clinical Oncology. 11(11):2112-7, 1993 Nov.

Return to top

N. Quality of life after autotransplants for breast cancer.

Ahles TA. Tope DM. Furstenberg C. Hann D. Mills L.
Psychologic and neuropsychologic impact of autologous bone marrow transplantation.
Journal of Clinical Oncology. 14(5):1457-62, 1996 May.

McQuellon RP. Muss HB. Hoffman SL. Russell G. Craven B. Yellen SB.
Patient preferences for treatment of metastatic breast cancer: a study of
women with early-stage breast cancer.
Journal of Clinical Oncology. 13(4):858-68, 1995 Apr.

Return to top

O. Hemopoetic stem cell sources for autotransplants for breast cancer.

de Graaf H. Mulder NH. Willemse PH. van der Graaf WT. Sleijfer DT.
Zijlstra JG. Elias M. Sibinga CT. Vellenga E. de Vries EG.
The additive effect of peripheral blood stem cells, harvested with
low-dose cyclophosphamide, to autologous bone marrow reinfusion on
hematopoietic reconstitution after ablative chemotherapy in breast cancer
patients with localized disease.
Anticancer Research. 15(6B):2851-6, 1995 Nov-Dec.

Elias AD. Ayash L. Anderson KC. Hunt M. Wheeler C. Schwartz G.
Tepler I. Mazanet R. Lynch C. Pap S. et al.
Mobilization of peripheral blood progenitor cells by chemotherapy and
granulocyte-macrophage colony-stimulating factor for hematologic support
after high-dose intensification for breast cancer.
Blood. 79(11):3036-44, 1992 Jun 1.

Myers SE. Mick R. Williams SF.
High-dose chemotherapy with autologous stem cell rescue in women with
metastatic breast cancer with involved bone marrow: a role for peripheral
blood progenitor transplant.
Bone Marrow Transplantation. 13(4):449-54, 1994 Apr.

Kritz A. Crown JP. Motzer RJ. Reich LM. Heller G. Moore MP. Hamilton
N. Yao TJ. Heelan RT. Schneider JG. et al.
Beneficial impact of peripheral blood progenitor cells in patients with
metastatic breast cancer treated with high-dose chemotherapy plus
granulocyte-macrophage colony-stimulating factor. A randomized trial.
Cancer. 71(8):2515-21, 1993 Apr 15.

Return to top

P. Autotransplants as outpatients.

Peters WP. Ross M. Vredenburgh JJ. Hussein A. Rubin P. Dukelow K.
Cavanaugh C. Beauvais R. Kasprzak S.
The use of intensive clinic support to permit outpatient autologous bone
marrow transplantation for breast cancer.
Seminars in Oncology. 21(4 Suppl 7):25-31, 1994 Aug.

Return to top

Q. Change in disease stage with extensive evaluation

Crump M. Goss PE. Prince M. Girouard C.
Outcome of extensive evaluation before adjuvant therapy in women with
breast cancer and 10 or more positive axillary lymph nodes.
Journal of Clinical Oncology. 14(1):66-9, 1996 Jan.
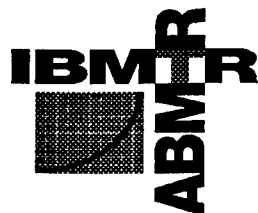
IBMTR / ABMTR

National and International Presentations
on Breast Cancer using ABMTR Data
1996-1997

January 1996

1996 IBMTR/ABMTR Participants' Meeting   Keystone, USA
J.O. Armitage: ABMTR update
K. Antman: Autotransplants for breast cancer

Keystone Symposium on Blood Cell and Bone Marrow Transplants   Keystone, USA
M.M. Horowitz: Analyzing transplant outcomes: comparison with other therapies
J.O. Armitage: Do autotransplants uniquely cure cancer?

February 1996

Cancer Care for Non-Oncologists   Irvine, USA
R.O. Dillman: Biotherapy for cancer

Blue Cross and Blue Shield Technology Center Forum   Chicago, IL
M.M. Horowitz: High dose chemotherapy versus autotransplants for breast cancer and multiple myeloma

March 1996

22nd Annual Meeting of the European Group for Blood and Marrow Transplantation   Vienna, Austria
M.M. Horowitz: Challenges in using observational data to compare treatment

California Society of Hospital Pharmacists   Newport Beach, USA
R.O. Dillman: New directions in stem cell transplants

4th International Symposium on Blood Cell Transplantation   Adelaide, South Australia
K.A. Antman: Blood cell transplants for breast cancer

Association of Cancer Executives   Philadelphia, USA
R.O. Dillman: Update on autologous BMT

April 1996

4th International Symposium on Blood Cell Transplantation   Adelaide, South Australia
K.A. Antman: Blood cell transplants for breast cancer

Association of Cancer Executives   Philadelphia, USA
R.O. Dillman: Update on autologous BMT

May 1996

American Society of Clinical Oncology   Philadelphia, USA
J.K. Erban: Effect of legislation mandating coverage for BMT for breast cancer
H.M. Lazarus: Outcome of autotransplants in older adults

Experimental and Clinical Approaches in Oncology: Approaching the 21st Century   Teaneck, USA
M.M. Horowitz: Use of blood and marrow transplant in cancer treatment

Societat Catalana de Hematologia   Barcelona, Spain
A. Julia: Indications of transplantation

June 1996

Indian Society of Hematology Meeting   Bombay, India
A.G. Mundia: Stem cell transplants in solid tumors

Advances in Haematology   London, UK
M.M. Horowitz: Use of blood and marrow transplantation in cancer treatment

August 1996

8th International Symposium on Autologous Marrow and Blood Transplantation   Arlington, USA
P.A. Rowlings: ABMTR results
P.A. Rowlings: Clinical studies in metastatic breast cancer

Joint Statistical Meetings   Chicago, USA
J.P. Klein: Modeling multistate survival illustrated in bone marrow transplantation

September 1996

Meeting of the American Academy of Insurance Medicine   Kansas City, USA
M.M. Horowitz: Outcome of blood and marrow transplantation

October 1996

Oncology Nursing Conference 1996   Santo Domingo, Dominican Republic
C. Meneghetti: High dose chemotherapy and autologous BMT for breast cancer treatment

22nd Annual Meeting of the Brazilian Society of Hematology and Hemotherapy   Porto Alegre, Brazil
D.G. Tabak: BMT in the Mercosul - A Brazilian perspective

November 1996

Second Uruguayan Congress on BMT and PBSC Transplants   Montevideo, Uruguay
G. Milone: Advances in breast cancer treatment: BMT results

Meeting of the Polish Society of Hematology   Poznan, Poland
J. Hansz: Past, present and future of hematopoietic cell transplantation

March 1997

I Encontro sobre Transplante de Medula Ossea e Hemopatias Malignas   Curitiba, Brazil
M.M. Horowitz: Breast cancer - ABMTR data

Annual Meetings of the BMT and Hematology Societies of Taiwan   Kaohseoug, Taiwan
C.H. Tzeng: An update on BMT and PBSCT

23rd Annual Meeting of the European Group for Blood and Marrow Transplantation   Aix-les-Bains, France
K. Antman: High-dose therapy for breast cancer in North America

1997 Blood Cell and Marrow Transplantation Multidisciplinary Symposium   Dallas, USA
P.A. Rowlings: Patient outcomes

April 1997

Canadian Apheresis Group Annual Meeting and Stem Cell Symposium   Quebec City, Canada
A. Keating: Overview of PBSC transplants

Brazilian College of Breast Surgeons   Rio de Janeiro, Brazil
D.G. Tabak: The role of BMT in the treatment of breast cancer

Bone Marrow Transplant Symposium   Graifswald, Germany
G. Dolken: High-dose chemotherapy as an adjuvant therapy for high-risk breast cancer

May 1997

Second National PBSCT Congress   Istanbul, Turkey
F. Arpaci: High-dose treatment in patients with solid tumors

American Society for Clinical Oncology   Denver, USA
M.M. Horowitz: Prognostic factors for outcome of autotransplants in women with high-risk breast cancer

November 1997

Dept. of Defense Breast Cancer Research Meeting   Washington, DC, USA
M.M. Horowitz: High-dose chemotherapy and blood or BMT for patients with high-risk breast cancer

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

MCMR-RMI-S   (70-1y)   4 Jan 00

MEMORANDUM FOR Administrator, Defense Technical Information
              Center, ATTN: DTIC-OCA, 8725 John J. Kingman
              Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has
reexamined the need for the limitation assigned to technical
reports written for the attached Grants. Request the limited
distribution statements for Accession Document Numbers listed be
changed to "Approved for public release; distribution unlimited."
This report should be released to the National Technical
Information Service.

2. Point of contact for this request is Ms. Judy Pawlus at
DSN 343-7322 or by email at Judy.Pawlus@amedd.army.mil.

FOR THE COMMANDER:

PHYLIS M. RINEHART
Deputy Chief of Staff for
    Information Management

95-1-5002   ADB235524

Completed 1-13-00 cc